26-7; 3-hydroxy-8-methylguanine, 30409-22-4; 3-hydroxy-7-methylguanine, 30345-27-8; 3-hydroxy-9-methylguanine, 30345-28-9; 1,7-dimethylguanine 3-oxide, 30345-29-0; 2-amino-6-methoxypurine 3-oxide, 30345-92-7.

Acknowledgment.—We thank for their helpfulness Drs. A. Albert and D. J. Brown of the John Curtin School of Medical Research, Australian National University, Canberra, where G. B. B. was a Fulbright and ANU Scholar in 1965. Drs. N. J. M. Birdsall, T. C. Lee, J. D. Fissekis, and S. Nesnow contributed many preliminary spectra and discussions. We thank Mr. Gerald Reiser for competent assistance.

Synthesis of 2-Thio-D-ribose and 2′-Thioadenosine Derivatives[1]

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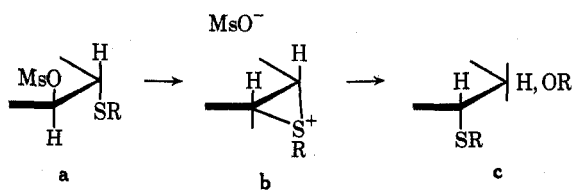
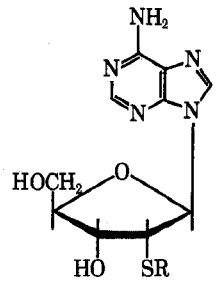
2-Thio-D-ribose derivatives, both furanose and pyranose, have been synthesized from the corresponding *S*-alkyl 1-thio-α-D-arabinoside 2-*O*-mesylates. The alkylthio group underwent stereospecific migration to C-2 with ejection of the *trans*-2-*O*-mesyl group. Depending on the medium, the 2-thio-D-ribose derivatives were obtained as methyl glycosides or as 1-*O*-acetates. In a deblocking sequence, methyl 2-thio-D-ribofuranoside was obtained as the free thiol. The *S*-methyl, *S*-benzyl, and tetrabenzoyl derivatives of 2′-thioadenosine were obtained from the furanose 1-*O*-acetates or their chloro sugars in reactions with purine bases. In some of the nucleoside condensations, 7-nucleosides were obtained as by-products and were identified by infrared and ultraviolet spectral properties, not previously reported, and characteristic of 7-substituted 6-benzamidopurines.

A number of new thio sugars have been synthesized in recent years, often for biological interest in their nucleoside derivatives. Of the positional isomers of thio-D-ribose, only 2-thio-D-ribose has not been synthesized previously. The requisite *cis*-3-OH,2-SH arrangement has not been achieved synthetically in any sugar, although numerous 2-thio sugars have been prepared with a trans mercapto–alcohol system. The *cis*-3-SH,-2-OH system of 3-thio-D-ribofuranose derivatives and 3′-thioadenosine was attained[2] only recently by the technique of internal displacement at C-3 with a *trans*-2-*O*-thionobenzoate. A related internal displacement at C-3 with a *trans*-2-*S*-thiolbenzoate was attempted[3] as a synthesis of 2-thio-D-ribofuranose but was unsuccessful; only the 2,3-episulfide was formed by neighboring participation of sulfur rather than oxygen.

The synthesis of 2-thio-D-ribose derivatives has now been accomplished in a related process by generating a 1,2-episulfonium ion (**b**) as intermediate. Starting from an *S*-alkyl 1-thio-α-D-arabinoside (**a**), with a readily displaced *trans*-*O*-mesylate at C-2 (and stable blocking groups at C-3 and at C-4 or C-5), the 1-alkylthio group underwent stereospecific migration to C-2. Ejection of the mesylate occurred with inversion at C-2 giving the D-ribo configuration, and the intermediate episulfonium ion (**b**) was opened by regiospecific attack at C-1 by a nucleophile provided by the medium. The 2-thio-D-ribose derivatives obtained by this means have been converted to the *S*-methyl, *S*-benzyl, and tetrabenzoyl derivatives (β-9-**33**, β-9-**31**, β-9-**29**) of 2′-thio-adenosine. 2′-Thioadenosine could not be obtained on deblocking. There was evidence for cleavage of the nucleoside link when the free thiol was liberated. Alternatively, 2′-*S*-methyl-2′-thioadenosine was selected as the target compound for study of biological properties.[4]





2′-thioadenosine, R = H
β-9-**33**, R = Me
β-9-**31**, R = CH_2Ph

The synthesis was studied first with pyranose sugars as models (Scheme I), owing to the ready availability of *S*-benzyl 1-thio-α-D-arabinopyranoside[5] (**3**) as starting material. The 3,4-*O*-cyclohexylidene acetal (**4**) was obtained as a crystalline substance and was used in preference to the isopropylidene analog, an oil. A 2-*O*-tosylate could not be formed from **4**, perhaps because of steric restrictions in this fused ring system. The 2-*O*-mesylate (**5**) was readily obtained; it could be stored at 5° for 1 week without deterioration but decomposed upon prolonged storage or on heating. Treatment of **5** with refluxing methanol containing sodium bicarbonate as acid acceptor caused nearly quantitative rearrangement to the methyl pyranoside **6** of 2-*S*-benzyl-2-

(1) This work was carried out under the auspices of the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, Public Health Service, Contract No. PH-43-64-500. The opinions expressed in this paper are those of the authors and not necessarily those of the Cancer Chemotherapy National Service Center.

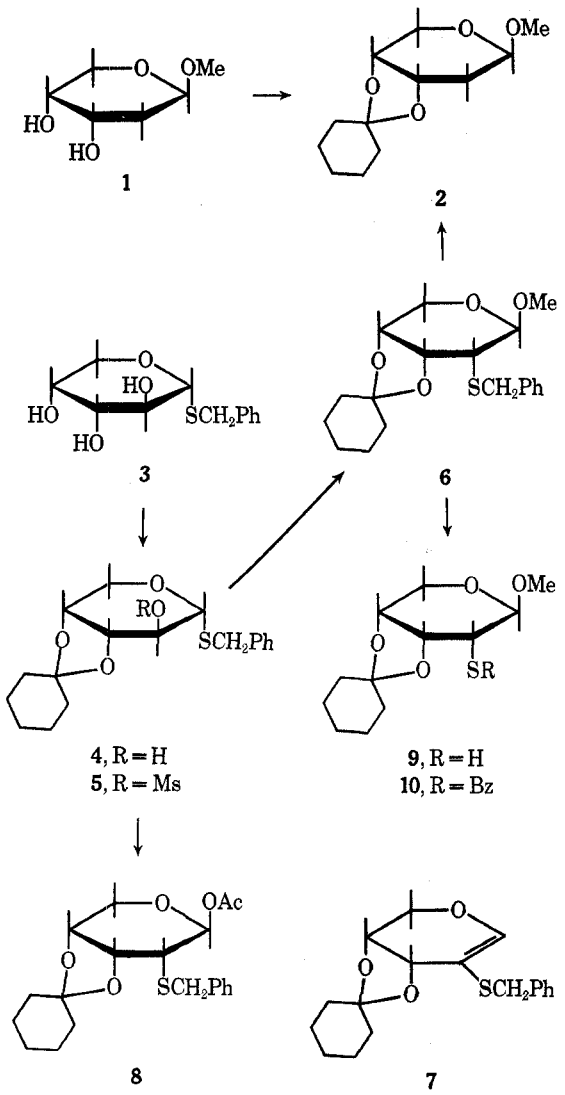
(2) K. J. Ryan, E. M. Acton, and L. Goodman, *J. Org. Chem.*, **33**, 1783 (1968).

(3) K. J. Ryan, E. M. Acton, and L. Goodman, *ibid.*, **33**, 3727 (1968).

(4) 2′-*O*-Methyl ribonucleosides have been found in RNA from a wide variety of sources. Although the biological function is unknown, it has been suggested that these may play an important role in protein biosynthesis: T. A. Khwaja and R. K. Robins, *J. Amer. Chem. Soc.*, **88**, 3640 (1966), and leading references.

(5) H. Zinner, A. Koine, and H. Nimz, *Chem. Ber.*, **93**, 2705 (1960).

SCHEME I



thio-D-ribose. Infrared and nmr spectra showed that the mesylate was completely ejected, and the nmr spectrum showed the presence of the 1-methoxyl. Clearly, the sulfur was now at C-2, from the distinctive upfield shift for H-2 at τ 7.37, where it appeared as a quartet coupled to H-1 (now shifted downfield at τ 5.21) and to H-3. The coupling constants indicated a trans diaxial relation between H-1 and H-2 (J = 7.5 Hz) and a cis axial–equatorial relation between H-2 and H-3 (J = 2.5 Hz), as expected[6,7] for the β-D-ribo configuration in a *C1* pyranose ring. Closer inspection of the nmr spectrum revealed 10–15% of the α anomer of **6**, from distinctive signals for OCH_3 and H-2. The anomers could be separated chromatographically; H-2 for the α anomer was a triplet, $J_{1,2} = J_{2,3}$ = 4 Hz, indicative of the equatorial–axial–equatorial arrangement. Topside attack at C-1 of **b** should have given the β anomer **6** exclusively; formation of some α anomer suggests that a carbonium ion developed to some extent at C-1. Desulfurization of **6** afforded crystalline methyl 3,4-*O*-cyclohexylidene-2-deoxy-β-D-ribopyranoside, identical with a sample synthesized independently from methyl 2-deoxy-β-D-ribopyranoside[8] (**1**). Debenzylation of **6** with sodium–liquid ammonia afforded the free thiol **9** in 86% yield. Benzoylation afforded the crystalline *S*-benzoate **10**.

Treatment of **5** with acetic anhydride–acetic acid containing potassium acetate afforded a mixture containing the β-1-*O*-acetate (**8**, 80% yield) of 2-*S*-benzyl-2-thio-D-ribopyranose, the α anomer (10%), and an olefin **7** (10%). Column chromatography effected a separation of **7** and **8**, following which **8** cystallized from methanol. A strong band at 6.22 μ in the infrared spectrum of **7** identified the olefin as a vinyl ether–vinyl sulfide, by comparison with other 2-*S*-alkyl-2-thio glycals.[9,10] Similarly, in the nmr spectrum, a sharp singlet at τ 3.42 was assigned to H-1 of structure **7** and confirmed that the benzylthio group was shifted to C-2. 2-*S*-Benzyl-3,4-*O*-cyclohexylidene-2-thio-D-arabinal (**7**) was presumably formed from the 1,2-episulfonium ion **b** by loss of the proton at C-2 and cleavage of the C-1–S bond. When the mesylate **5** was treated with sodium benzoate in hot dimethylformamide, the olefin **7** was the main product, with only 16% of the β-1-*O*-benzoate analogous to **8**.[11] A related olefin, 2-(*N*,*N*-dimethyldithiocarbamoyl)-D-glucal, was recently obtained[12] from a 2-*O*-mesyl-β-D-glucopyranosyl *N*,*N*-dimethyldithiocarbamate; ejection of the mesylate by sulfur was accomplished through a five-membered cyclic intermediate analogous to **b**.

In furanose series (Scheme II) the requisite *S*-alkyl 1-thio-D-arabinofuranosides (**13** and **14**) with the 2-OH free for mesylation were best obtained from 1,3,5-tri-*O*-benzoyl-D-arabinofuranose[13] (**11**). This was a better source of the 2-hydroxy chloro sugar **12** than was 3,5-di-*O*-benzoyl-D-arabinose.[14] When the chloro sugar **12** was treated with an equivalent amount of sodium benzyl mercaptide, a high degree of steric control was exerted, possibly by the 2-hydroxyl. Benzyl 3,5-di-*O*-benzoyl-1-thio-α-D-arabinofuranoside (**13**) was obtained, contaminated with very little of the β anomer. Pure **13** could be obtained free of the anomer and other impurities by crystallization in 25% yield. The 2-*O*-mesylate **15** was converted in nearly quantitative yields to the 1-*O*-methyl (**23**) or 1-*O*-acetyl (**17**) derivatives of 2-thio-D-ribose. The formation of **23** was done in methanol containing silver carbonate and Drierite, to avoid the debenzoylation at C-3 and C-5 which had occurred with methanol and sodium bicarbonate.

The stringent requirement for a trans relation between the 2-*O*-mesyl and 1-benzylthio groups in these migration–inversions was demonstrated in one experiment when 2-*O*-mesylate **15** from crude **13** was used, containing a little β anomer; this anomer of **15** survived unchanged in the reaction to form the 1-*O*-acetate **17**, as predicted for a *cis*-2-*O*-mesylate. With the migration–inversion in the furanose series, there was no

(6) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *J. Amer. Chem. Soc.*, **80**, 6098 (1958).

(7) C. V. Holland, D. Horton, M. J. Miller, and N. S. Bhacca, *J. Org. Chem.*, **32**, 3077 (1967).

(8) R. E. Deriaz, W. G. Overend, M. Stacey, and L. F. Wiggins, *J. Chem. Soc.*, 2836 (1949).

(9) U. G. Nayak, M. Sharma, and R. K. Brown, *Can. J. Chem.*, **45**, 481 (1967).

(10) U. G. Nayak, M. Sharma, and R. K. Brown, *ibid.*, **45**, 1767 (1967).

(11) A preliminary report of some of this work was made: K. J. Ryan, E. M. Acton, and L. Goodman, Abstracts of the 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1968.

(12) S. Ishiguro and S. Tejima, *Chem. Pharm. Bull.*, **15**, 1478 (1967).

(13) R. K. Ness and H. G. Fletcher, Jr., *J. Amer. Chem. Soc.*, **80**, 2007 (1958).

(14) E. J. Reist, P. A. Hart, L. Goodman, and B. R. Baker, *ibid.*, **81**, 5176 (1959).

SCHEME II

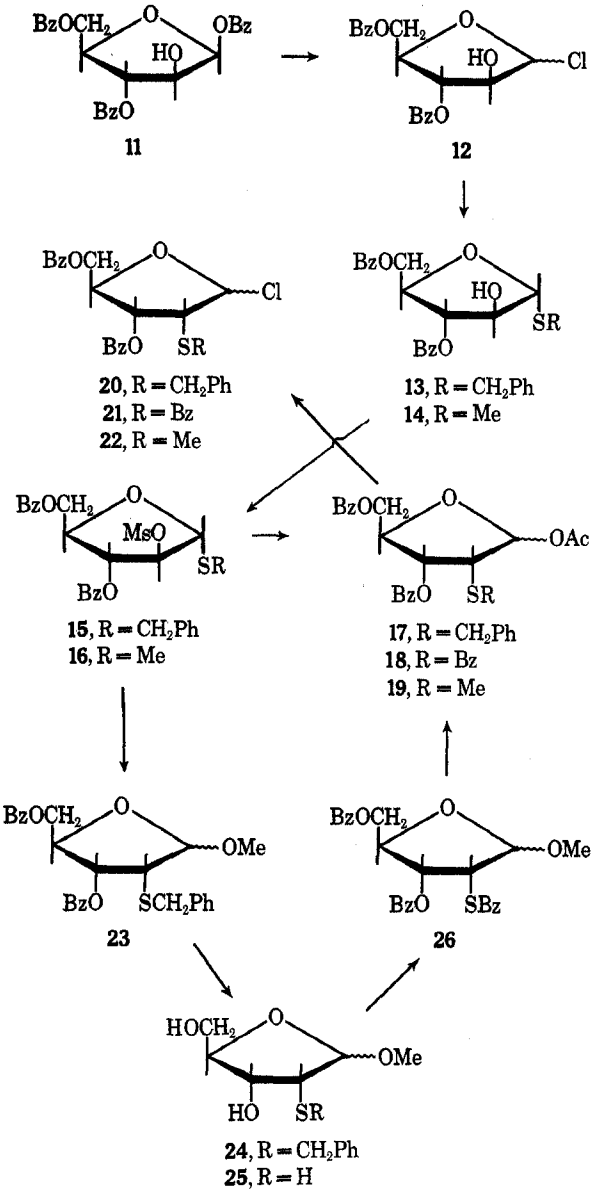
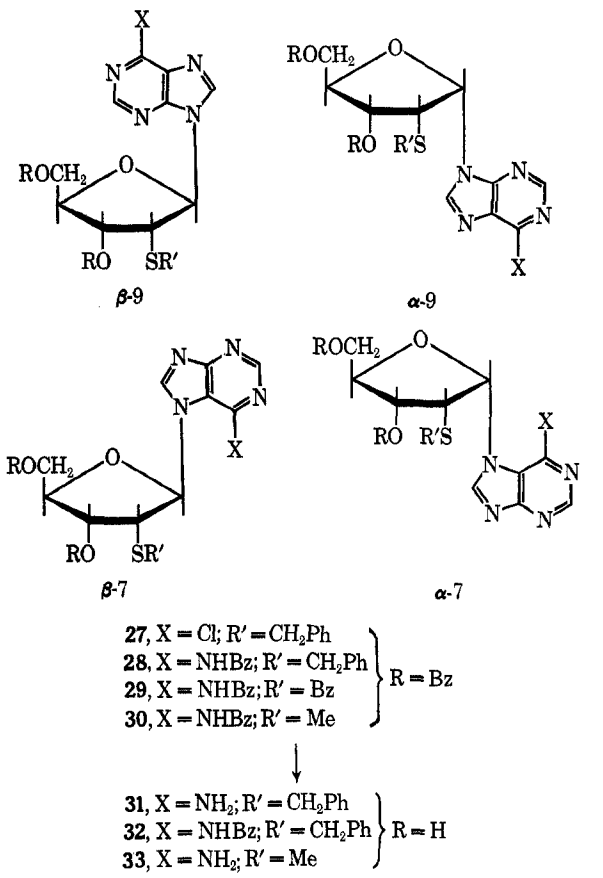


TABLE I

CORRELATION OF NMR DATA FOR 2-THIO-D-RIBOFURANOSES

Compd	β-C-1-H τ	β-C-1-H $J_{1,2}$, Hz	α-C-1-H τ	α-C-1-H $J_{1,2}$, Hz	$J_{2,3}$, Hz β	$J_{2,3}$, Hz α
17	3.63 d	2.5	3.54 d	4.5	6.8	6.8
18	3.49 d	3.0	3.28 d	4.7	6.3	6.7
19	3.63 d	2.0	3.40 d	4.7	6.5	6.4
23	4.98 d	3.1	5.11 d	4.8	6.4	7.0
24	5.16 d	3.4	5.17 d	5.0	5.6	6.4
25	5.09 d	2.8	5.04 d	5.0		
26	4.79 d	2.8		4.9	6.2	6.8

SCHEME III



evidence that a 1,2 olefin like **7** was formed. Both the products **17** and **23** contained appreciable amounts of α anomers. The anomers were identified from the coupling constants in the nmr, based on the statement[15] that values "less than about 4 Hz may be ascribed to neighboring trans hydrogens." The nmr was a consistently useful tool for structure confirmation of all the 2-thio-D-ribofuranoses in Scheme II that could be measured (**17** through **19**, **23** through **26**; see below for chemistry of the *S*-benzoyl and *S*-methyl compounds). As shown in Table I, $J_{1,2}$ values for the β anomers were consistently 2.0–3.0 Hz and for the α anomers were 4.5–5.0 Hz. With the 1-*O*-acetates (**17**, **18**, **19**), the α-C-1-H was shifted noticeably downfield from the β-C-1-H, in accord with an observation made[15] on a number of 1-*O*-acyl furanoses that "H-1 is at lower field when the substituents are cis." For compounds **17** and **19**, the location of H-2 upfield from the other sugar protons showed that the sulfur was at C-2 (with the *S*-benzoyl compounds the upfield shift was less obvious). That $J_{2,3}$ was 5.6–7.0 Hz was regarded as confirming evidence for the ribo configuration (2,3-cis[15]), especially in contrast with $J_{2,3}$ values of 1.9 Hz for an *S*-benzyl 2-thio-D-xylofuranoside[16] and 3.9 or 2.6 Hz for an *S*-benzyl 2-thio-D-arabinoside[17] (2,3-trans).

The nucleoside syntheses undertaken (Scheme III) are summarized in Table II. Fusion of the 1-*O*-acetate **17** with 6-chloropurine and chloroacetic acid catalyst was studied first. The nucleoside 9-**27** obtained was a mixture of β and α anomers in a ratio of about 2:1. Again, the anomeric configurations could be determined by nmr. Eventually it was found that *with all the 6-substituted 9-purinyl nucleosides of 2'-thio-D-ribose examined in this work, $J_{1',2'}$ = 9.0–9.5 Hz for β anomers and 7.0–7.5 Hz for α anomers.* These values are larger than normally observed with adenosine derivatives, and perhaps this is due to the presence of sulfur at C-2'. The α anomer (α-9-**27**) could be crystallized from the α,β mixture, and amination–deacylation afforded crystalline 9-(2-*S*-benzyl-2-thio-α-D-ribofuranosyl)adenine (α-9-**31**). Amination–deacylation of the

(15) J. D. Stevens and H. G. Fletcher, Jr., *J. Org. Chem.*, **33**, 1799 (1968).

(16) G. Casini and L. Goodman, *J. Amer. Chem. Soc.*, **86**, 1427 (1964).

(17) L. Goodman, *ibid.*, **86**, 4167 (1964).

TABLE II

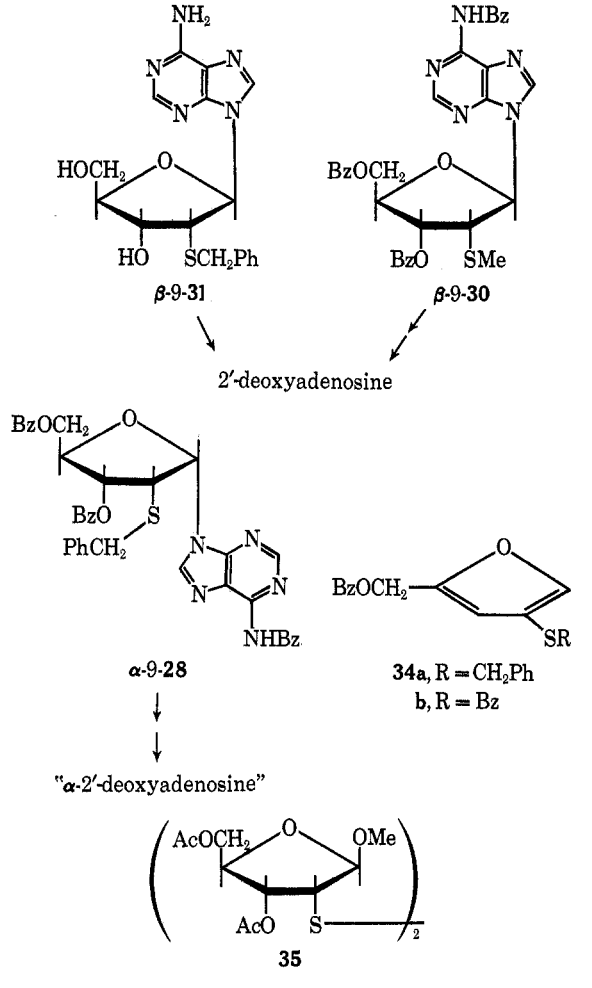
SUMMARY OF NUCLEOSIDE CONDENSATIONS

Sugar	Purine	Method	Products		
17	6-Cl-purine	Fusion	β-9-27 (25)[a]	α-9-27 (13)[a]	
20	6-BzNH-purine	Molecular sieve	β-9-28 (0.6)[a]	α-9-28 (5.4)[a]	
20	Bis(Me_3Si)-6-BzNH-purine	$HgBr_2$[b]	β-9-28 (22)[a]	α-9-28 (5)[a]	7-28[c] (9)[a]
21	Bis(Me_3Si)-6-BzNH-purine	$HgBr_2$[d]	β-9-29 (25)[e]		7-29[c] (estimated 5)
22	Bis(Me_3Si)-6-BzNH-purine	$HgBr_2$[b]	β-9-30 (34)[e]	α-9-30 (10)[e]	7-30 (12)[e,f]

[a] Per cent in parentheses determined by nmr analysis of the isolated α,β mixture. [b] Without isomerization by heating. [c] Anomeric composition could not be determined. [d] With heating to isomerize the 7 isomer to the 9 isomer. [e] Per cent isolated. [f] Both anomers present, one of which crystallized (6%).

mother liquor from α-9-**27**, enriched in β-9-**27**, afforded a mixture from which crystalline 2′-*S*-benzyl-2′-thioadenosine (β-9-**31**) and some additional α-9-**31** could be separated by chromatography. Structure proof at this point depended on ultraviolet spectra (*vide infra*), which verified that both anomers were 9-nucleosides, and on desulfurization of β-9-**31** to give 2′-deoxyadenosine. A by-product from the fusion, which had to be separated first by chromatography, was the furan **34a**, presumably obtained by elimination of acetic acid plus benzoic acid from **17**. This elimination became overwhelming in larger scale reactions, and the fusion process could not be pursued.

Attempts to prepare a chloro sugar **20** from the 1-*O*-acetate **17** by conventional treatment with ethereal hydrogen chloride at 0° produced a tar. At −60°, however, the preparation of **20** was entirely straightforward, and a variety of other nucleoside syntheses could be studied. Mild treatment of the chloro sugar **20** with 6-benzamidopurine in the presence of a molecular sieve as acid acceptor[18,19] afforded a nucleoside that proved to be mainly α-9-**28**, judging from the $J_{1',2'}$ of 7.0 Hz and from the deacylation to crystalline α-9-**31**. The most successful nucleoside synthesis in this work was based on a recent procedure[20] for treating a chloro sugar with bis(trimethylsilyl)-6-benzamidopurine in benzene solution containing mercuric bromide. It was reported that a significant proportion of 7-nucleoside was formed along with 9-nucleoside, but that isomerization to the 9 isomer could be accomplished with heating, and that the anomeric configuration was largely β. The 2-*S*-benzyl chloro sugar **20** in this procedure afforded, after 6 days at room temperature, a mixture containing about 27% of the blocked 9-nucleoside (9-**28**, with a β:α ratio of 4:1) and about 9% of the blocked 7-nucleoside (7-**28**). These isomers could be separated chromatographically. Normal ultraviolet (Table III) and infrared spectra were observed for 9-**28**; the anomeric composition was determined as mainly β from the $J_{1',2'}$ values in the nmr. This identity was confirmed on debenzoylation to give crystalline 2′-*S*-benzyl-2′-thioadenosine (β-9-**31**), identical with that from β-9-**27** above. The blocked 7-nucleoside (7-**28**) was clearly distinguished by characteristic ultraviolet absorption maxima (*vide infra*) and by extraordinary and unexpected infrared bands. The unusual infrared bands (most notably a strong, sharp peak at 6.08 μ which could be easily detected even in mixtures) were observed with all the 7-substituted nucleosides of 6-benzamidopurine studied in this work and seem not to have been reported previously. The anomeric composition of 7-**28** (as one or both possible anomers) could not be estimated from the nmr, since the signal for H-1′ was apparently obscured by aryl protons.

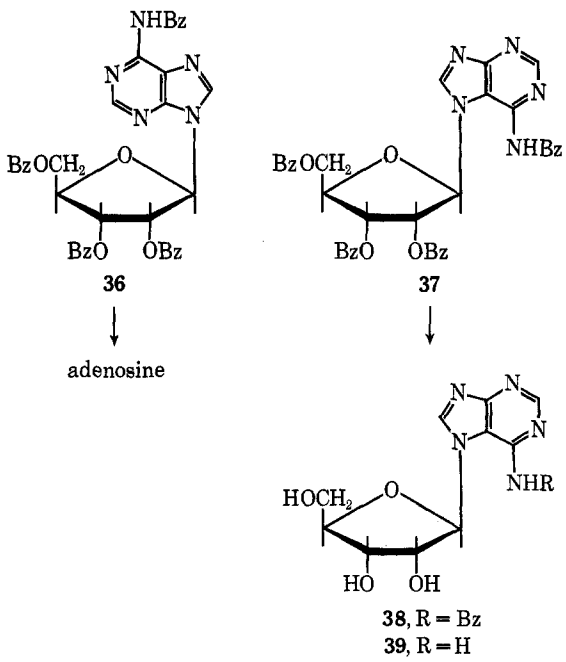


Debenzoylation of 7-**28** afforded two products, which could be separated by chromatography, and which crystallized. The chromatographically less mobile product was identified as 7-(2-*S*-benzyl-2-thio-D-ribofuranosyl)-7*H*-adenine (7-**31**) by the characteristic ultraviolet

(18) C. P. J. Glaudemans and H. G. Fletcher, Jr., *J. Org. Chem.*, **28**, 3004 (1963).
(19) F. Keller, I. J. Botvinick, and J. E. Bunker, *ibid.*, **32**, 1644 (1967).
(20) B. Shimizu and A. Saito, *Agr. Biol. Chem. (Tokyo)*, **33**, 119 (1969).

absorption for 7-substituted adenines[21,22] (Table III). Although the anomeric configuration of 7-**31** could not be determined from the nmr spectrum, it crystallized presumably as a single anomer. The other, more mobile product was not simply the anomer of 7-**31**. Elemental analysis showed, rather, that it was a benzoyl derivative of 7-**31**, incompletely deblocked. That it was the 6-*N*-benzoyl derivative 7-**32** was indicated by the unusual infrared bands (including a strong, sharp band at 6.10 μ) for a 7-substituted 6-benzamidopurine. The ultraviolet maxima (Table III) at pH 7 and 13 resembled those of the fully benzoylated 7-nucleosides and were distinct from those of the fully benzoylated 9-nucleosides. The ultraviolet maxima at pH 1 resembled those of 6-benzamidopurine itself. At pH 1, there was, in fact, rapid cleavage of 7-**32** to 6-benzamidopurine, owing to a very high degree of acid sensitivity. The presence and position of benzoyl attachment in 7-**32** was thereby confirmed. Such acid sensitivity was not found with the fully blocked precursor 7-**28** or any of the other classes of nucleosides in this study. However, the 2′-thionucleoside derivatives seemed generally less stable than their D-ribose analogs. Attempts to isomerize a mixture of the fully blocked nucleosides (9-**28** and 7-**28**) to the 9 isomer gave a competing elimination of the purine moiety to the furan derivative **34a**, which became predominant in refluxing xylene containing mercuric bromide, as directed[20] for the ribose analogs.

Since the properties of the 7-nucleosides (7-**32** and 7-**28**) derived from 6-benzamidopurine were somewhat novel, the nucleoside condensation with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide was repeated,[20] and a sample of crystalline 6-benzamido-7-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-7*H*-purine (**37**) was isolated for comparison. Unusual, distinguishing features of the ultraviolet and infrared spectra were like those of



the 2′-benzylthio analog 7-**28**. Further, debenzoylation with methanolic sodium methoxide gave 7-β-D-ribofuranosyladenine (**39**), along with the crystalline 6-*N*-benzoyl derivative **38**. As before, these were conditions that, with the 9 isomers, gave complete deblocking. The spectral properties and acid sensitivity of 6-benzamido-7-β-D-ribofuranosyl-7*H*-purine (**38**) matched those of the 2-benzylthio analog 7-**32**. This product was apparently not observed in the previous deblocking[20] of **37**. (Assignment of the β anomeric configuration to **37**, **38**, and **39** was based on the previous[20] determination with amorphous **37**.)

The preparation of 2′-thioadenosine from β-9-**31** was attempted by S-debenzylation with sodium–liquid ammonia, but no nucleoside could be detected in the product, and the only isolable fragment was adenine. For this reason, an *S*-benzoyl precursor (*i.e.*, β-9-**29**) was sought as being susceptible to milder deblocking. The *S*-benzyl blocking group was exchanged for an *S*-benzoyl group in the sugar precursors (Scheme II). Methyl 3,5-di-*O*-benzoyl-2-*S*-benzyl-2-thio-α,β-D-ribofuranose (**23**) was converted to methyl 2-thio-α,β-D-ribofuranoside (**25**), which was benzoylated to give **26**. The intermediate thiol **25** was obtained from a sodium–liquid ammonia debenzylation in high yield by extraction and was characterized by its spectra. There was no observed tendency toward elimination or even toward disulfide formation when it was protected from air. Acetolysis of methyl 2-*S*-benzoyl-3,5-di-*O*-benzoyl-2-thio-α,β-D-ribofuranoside (**26**) gave blackening and decomposition when attempted at $-5°$ but at $-20°$ gave the 1-*O*-acetate **18** in nearly quantitative yield. Conversion to the chloro sugar **21** occurred at $-60°$, also in quantitative yield. Condensation of **21** with bis(trimethylsilyl)-6-benzamidopurine in benzene in the presence of mercuric bromide gave a mixture of 7- and 9-nucleosides **29** in roughly comparable amounts, judging from the intensities on thin layer chromatography and from the characteristic infrared bands for 7 isomers. If the reaction mixture was refluxed prior to its work-up, the 7 isomer was isomerized almost completely to β-9-**29**, the tetrabenzoyl derivative of 2′-thioadenosine; there was little elimination to form a furan (presumably **34b**). Chromatographic purification afforded β-9-**29** in 25% yield. The characteristic $J_{1',2'}$ of 9.0 for β-9 anomers was observed in the nmr spectrum, with no evidence for the α anomer. All attempts to prepare 2′-thioadenosine by debenzoylation of β-9-**29** in alkaline methanol afforded adenine as the only detectable purine derivative. In one experiment, the water-soluble sugar fragment was recovered and was acetylated; it consisted entirely of methyl 3,5-di-*O*-acetyl-2-thio-β-D-ribofuranose obtained as the disulfide **35**. The complete cleavage of the nucleoside whenever the 2′-SH was liberated suggested that the thiol (or its anion) acted to eject the purine base, which is situated in the trans position on the adjacent carbon. Probably this occurred through a 1,2-episulfide; attack by solvent methanol at C-1 then gave the methyl β-D-furanoside. These results suggest that 2′-thioadenosine, if ever isolated, would be highly unstable, at least in base.

Finally, synthesis of 2′-*S*-methyl-2′-thioadenosine (β-9-**33**) was carried out by the sequence used for the *S*-benzyl analog β-9-**32**. Methyl 3,5-di-*O*-benzoyl-1-thio-α-D-arabinofuranoside (**14**) was obtained in much better yield than the benzyl analog **13**, since a large excess of methanethiol could be used advantageously

(21) N. J. Leonard and J. A. Deyrup, *J. Amer. Chem. Soc.*, **84**, 2148 (1962).

(22) J. A. Montgomery and H. J. Thomas, *ibid.*, **87**, 5442 (1965).

TABLE III
ULTRAVIOLET SPECTRA OF ADENINE NUCLEOSIDES

Compd (2′ substituent)	λ_{max} mμ (ε × 10⁻³) pH 1	pH 7	pH 13
	A. 9-Nucleosides, Fully Benzoylated[a]		
β-9-**28** (SCH_2Ph)	206 (42.7), 237 (37.1), 293 (28.1)	208 (41.7), 233 (34.5), 287 (28.1)	218 (51.5), 275 sh, 304 (12.8)
β-9-**29** (SBz)	208 (44.5), 242 (38.5), 287 (33.1)	207 (48.0), 237 (39.0), 281 (30.4)	218 (56.3), 276 sh, 303 (13.8)
β-9-**30** (SMe)	238 (28.2), 294 (24.3)	207 (40.7), 238 (34.6), 286 (25.4)	218 (60.2), 276 sh, 304 (13.5)
36 (OBz)[b]	204 (45.7), 237 (38.0), 279 (20.9), 284 (21.1)	208 (37.5), 238 (33.4), 279 (19.9), 284 (20.0)	219 (45.6), 264 sh, 303 (9.74)
	B. 7-Nucleosides, Fully Benzoylated[a]		
7-**28** (SCH_2Ph)	208 (38.6), 242 (35.7), 338 sh, 349 (26.2)	207 (50.3), 238 (40.4), 338 sh, 348 (24.7)	319 (11.0)
7-**29** (SBz)	206 (44.5), 238 (34.2), 278 sh, 335 (15.9), 348 (16.0)	203 (52.2), 235 (35.7), 278 sh, 335 (14.6), 347 (14.2)	272 (10.0), 301 (9.10)
7-**30** (SMe)	230 (43.4), 332 (20.8)	207 (37.9), 238 (33.9), 345 (21.1)	325 (14.9)
37 (OBz)[c]	207 (42.5), 242 (37.3), 338 sh, 350 (22.4)	238 (40.5), 338 sh, 345 (21.7)	276 sh, 321 (11.8)
	C. 7-Nucleosides, Mono-*N*-benzoyl[d]		
7-**31** (SCH_2Ph)	251 (11.3), 287 (20.0)	335 (14.0)	325 (11.3)
38 (OH)	251 (9.45), 287 (20.0)	228 (14.3), 330 (18.0)	324 (13.2)
	D. Purines		
6-Benzamidopurine	251 (10.2), 288 (23.2)	235 (11.8), 248 (11.6), 286 (19.1)	279 (12.0)
Adenine	263 (13.1)		269 (12.3)
	E. 9-Nucleosides (Deacylated)[a]		
β-9-**32** (SCH_2Ph)	260 (13.5)	261 (14.4)	260 (14.2)
α-9-**32** (SCH_2Ph)	259 (11.4)	261 (12.0)	261 (12.2)
β-9-**33** (SMe)	258 (15.0)	260 (14.6)	260 (15.5)
α-9-**33** (SMe)	258 (14.3)	260 (14.2)	260 (15.5)
Adenosine	257 (14.6)	260 (14.4)	260 (14.9)
	F. 7-Nucleosides (Deacylated)[a]		
7-**32**	220 sh, 273 (10.7) [λ_{min} 240 (5.00)]	245 sh, 272 (7.80) [λ_{min} 234 (5.45)]	245 sh, 272 (7.45) [λ_{min} 240 (5.75)]
39[e]	273 (12.0) [λ_{min} 240 (4.20)]	245 sh, 270 (8.15) [λ_{min} 232 (4.00)]	245 sh, 270 (8.50) [λ_{min} 234 (4.95)]

[a] Stock solution prepared in ethanol and then diluted 1/10 with aqueous buffers; when the stock solution was in EtOH–water (1:1) containing 0.05 *M* HCl and then diluted with buffers, there were no significant changes in the spectra. [b] The spectrum in neutral ethanol lacked the maximum at 284 mμ and was as reported in ref 20. [c] The spectrum in neutral ethanol showed maxima at 231 and 330 mμ, as reported in ref 20; the absorption maxima beyond 300 mμ are generally less striking in ethanol than in water. [d] Stock solution prepared in ethanol and then diluted 1/10 with aqueous buffers; the maximum at pH 1 is attributed to 6-benzamidopurine formed by acid cleavage; when the stock solution was in EtOH–water (1:1) containing 0.05 *M* HCl, dilution with pH 7 and with pH 13 then also gave solutions with the maxima of 6-benzamidopurine. [e] See also ref 21 and 22.

along with its sodium salt in the reaction[14] with 3,5-di-*O*-benzoyl-D-arabinofuranosyl chloride (**12**), without concern about removing the disulfide formed. Purification of **14** or of its 2-*O*-mesylate **16**, both oils, was unnecessary before migration–rearrangement to give the 1-*O*-acetyl-2-*S*-methyl-2-thio-D-ribofuranose **19**. The acetate **19** was purified by chromatography and obtained as an α:β mixture (40:60). The β anomer could be separated by crystallization, but the anomeric mixture was equally good for conversion, again at Dry Ice temperatures, to the chloro sugar **22**. On treatment with bis(trimethylsilyl)-6-benzamidopurine and mercuric bromide, the nucleoside **30** was obtained predictably as a mixture of 7 and 9 isomers. In this case, both 7-**30** and 9-**30** were seen to be mixtures of their α and β anomers. In a run where there was no attempt at 7 → 9 isomerization by heating the reaction mixture, chromatography separated 34% of β-9-**30**, 10% of α-9-**30**, and 12% of α,β-7-**30** as an anomeric mixture. The β-9 and α-9 anomers were immediately differentiated in the nmr by $J_{1',2'}$ values of 9.0 and 7.0 Hz, respectively. Reliability of this means of assignment was again confirmed by desulfurization and debenzoylation of β-9-**30** to 2′-deoxyadenosine. The differentiation in coupling constants for the 9 isomers still held after debenzoylation to 2′-*S*-methyl-2′-thioadenosine (β-9-**33**, $J_{1'2'}$ = 9.0 Hz) and its α anomer (α-9-**33**, $J_{1',2'}$ = 7.0 Hz). These nucleosides were isolated through the picrate salts, and 2′-*S*-methyl-2′-thioadenosine was thereby obtained as a cystalline solid.

The $J_{1',2'}$ values could be determined for the anomers present in 7-**30**, but any assignment of their anomeric configuration was highly speculative. The major anomer could be crystallized and was debenzoylated to a cystalline nucleoside (one of the anomers of 7-**33**).

Ultraviolet Spectra.—Certain common features in the ultraviolet spectra were characteristic for each class of nucleosides (Table III) and served to distinguish them. For example, the fully benzoylated 9-nucleosides at pH 1 and 7 all exhibited maxima at 281–287 mμ, reminiscent of the absorption for 6-benzamidopurine. In contrast, the fully benzoylated 7-nu-

cleosides at pH 1 and 7 lacked a peak near 285 mμ but showed rather unexpected maxima at 335–338 mμ (sometimes a shoulder) and at 345–350 mμ. In all previous studies, adenine derivatives have generally not shown ultraviolet maxima much beyond 300 mμ. These maxima are apparently restricted to 7-substituted 6-*N*-acyladenines. Examples previously recorded without comment were **37**,[20] 6-*N*-benzoyl-7-benzyladenine,[23] and 6-*N*-pivaloyl-7-pivaloyloxymethyladenine.[24] The 9 and 7 isomers were more similar at pH 13, in presumably anionic forms; the spectra showed maxima at 303–304 and at 301-325 mμ, respectively. The unusual maxima at 330 and 335 mμ were retained in the mono-*N*-benzoyl 7-nucleosides **7-32** and **38** at pH 7. The high degree of acid sensitivity of these compounds was exhibited at pH 1, where the spectrum nearly coincided with that for 6-benzamidopurine. The rapid cleavage of the nucleoside link was further demonstrated when these compounds were dissolved in ethanol–0.1 *N* hydrochloric acid (1:1) as a stock solution followed by the usual dilution with appropriate buffers (Table III, footnote *d*). The other nucleosides were unaffected by acid in this treatment (Table III, footnote *a*). All the nucleosides appeared to be stable in base while the spectra were run. With the free, deacylated nucleosides, maxima of the 9 isomers near 260 mμ were characteristic for adenosine analogs. Maxima near 272 mμ were typical of either 7- or 3-substituted adenines, and the 7-nucleosides were characterized as such by the difference[21,22] between λ_{min} at pH 1 and at pH 7.

Experimental Section

Methods.—Melting points were determined on a Fisher-Johns hot stage and are uncorrected. Optical rotations were measured on 1% solutions in 1-dm tubes with a Perkin-Elmer Model 141 automatic polarimeter. Thin layer chromatography (tlc) was done with silica gel HF (E. Merck, Darmstadt) on 5 × 20 cm glass plates. The spots were detected under ultraviolet light. Preparative tlc was done with silica gel of 1 or 2 mm thickness on 20 × 20 cm plates. With multiple elutions, the plates were dried each time. In processing reactions, the bicarbonate solution used was saturated aqueous sodium bicarbonate. Organic solutions were dried with magnesium sulfate, which was removed by filtration. The Celite filter aid, used where mentioned, was a diatomaceous earth. Solutions were concentrated or evaporated *in vacuo* with a spin evaporator. Anhydrous tetrahydrofuran (THF) was distilled from calcium hydride.

Spectra Determination.—Ultraviolet spectra were determined with a Cary Model 11 recording spectrophotometer. Infrared spectra were determined routinely, as liquid film, or in Nujol mull for solids. Only bands important for structure assignment are reported. *O*-Benzoates generally showed stong bands near 5.8, 7.9, and 14.0 μ, even if not listed. *S*-Benzoates showed bands near 5.95, 8.3, 11.0, and 14.5 μ. *O*-Acetates and *O*-mesylates also showed the expected absorption bands. Nmr spectra were determined in chloroform-*d* solutions, unless otherwise noted, using 1% tetramethylsilane (τ 10.00) as internal reference (or as external reference with D_2O) with Varian A-60A and HR-100 spectrometers. Signals are described as singlet (s), doublet (d), triplet (t), quartet (q), or multiplet (m). Accuracy was ±0.05 ppm for chemical shifts and ±0.2 Hz for coupling constants. Integrated signal ratios were determined routinely and were as expected from the structural assignments. Benzoates commonly showed multiplets at τ 1.8–2.1 (2 aryl H's) and 2.3–2.7 (3 aryl H's), not listed for each compound. The cyclohexylidene compounds in Scheme I all showed signals at τ 8.1–8.8 (ring CH_2). The purines generally showed two singlets for H-2 and H-8, but these could not be individually assigned.

A. Pyranose Series. Benzyl 3,4-*O*-Cyclohexylidene-1-thio-α-D-arabinopyranoside (4).—To a solution of 18 g (70 mmol) of benzyl 1-thio-α-D-arabinopyranoside (**3**), mp 105–110° (lit.[5] 109°), in 225 ml of dry dimethylformamide was added 10.5 ml (123 mmol) of cyclohexanone, 22.5 ml (170 mmol) of triethyl orthoformate, and 0.5 ml of dioxane that had been saturated with hydrogen chloride.[25] The mixture was stirred at room temperature for 18 hr, neutralized with Dowex 2 (CO_3) ion exchange resin, and filtered. The filtrate was evaporated to dryness. The residue was mixed and extracted with 500 ml of refluxing cyclohexane. The hot cyclohexane was decanted and evaporated. The residue was dissolved in 100 ml of hot methanol, and water was added to the cloud point. The solution, clarified with a little more methanol, was seeded and chilled to yield 14.5 g (62%), mp 91–93°. Seed crystals and a sample for analysis were obtained in a previous experiment by preparative tlc in benzene–ether (9:1): mp 94–95.5°; $[\alpha]^{22}D$ +69° ($CHCl_3$); nmr τ 2.71 s (C_6H_5), 6.12 s (SCH_2Ph). Signals for the sugar ring protons were at τ 5.5–6.6 and could not be analyzed; the complex pattern within this narrow range appeared to be concentration dependent. A second crystal form was isolated, mp 122–123°, mmp 121–123°, and there was no change in optical rotation.

Anal. Calcd for $C_{18}H_{24}O_4S$: C, 64.3; H, 7.19; S, 9.53. Found: C, 64.2; H, 7.10; S, 9.80.

Benzyl 3,4-*O*-Cyclohexylidene-2-*O*-methanesulfonyl-1-thio-α-D-arabinopyranoside (5).—A stirred solution of 3.0 g (9.0 mmol) of **4** in 30 ml of pyridine was chilled to 0°, treated with 3.0 ml (18 mmol) of methanesulfonyl chloride, and stored at −5° for 18 hr. The chilled solution was stirred and treated dropwise during 5–10 min with 2 ml of water. Stirring was continued for 1 hr, and the mixture was partitioned between 200 ml of bicarbonate solution and 100 ml of chloroform. The chloroform layer was separated, washed with 100 ml of water, dried, and concentrated (bath not over 40°). The residual oil, 4.3 g, was used immediately or stored at −5°: nmr (C_6D_6) τ 2.84 m (C_6H_5), 5.16 q (2-H), 5.83 d (1-H), 5.96 q (5-H, eq), 6.05–6.3 (3-H, 4-H, SCH_2Ph), 6.81 q (5-H, ax), 7.27 s (OSO_2CH_3), $J_{1,2}$ = 9.0 Hz, $J_{2,3}$ = 6.5, $J_{3,4}$ estimated 5.1, $J_{4,5a}$ = 3.0, $J_{4,5e}$ = 2.5, $J_{5a,5e}$ = 12.5 Hz. If the reaction mixture was hydrolyzed by fast addition of water, there was heating and concomitant elimination to **7**, as evidenced by the ir absorption band at 6.22 μ.

Methyl 2-*S*-Benzyl-3,4-*O*-cyclohexylidene-2-thio-β-D-ribopyranoside (6).—A solution of the syrupy mesylate **5** (9 mmol, based on **4**) in 125 ml of anhydrous methanol was treated with 2.5 g (30 mmol) of solid sodium bicarbonate. The mixture was refluxed for 5 hr and evaporated to dryness. The residue was partitioned between 50 ml of chloroform and 50 ml of water. The chloroform extract was washed with 50 ml of water, dried, and concentrated to a residual oil, which was dried *in vacuo* at room temperature, 3.1 g (98%).

Anal. Calcd for $C_{19}H_{26}O_4S$: C, 65.1; H, 7.48; S, 9.15. Found: C, 64.9; H, 7.30; S, 9.44.

The nmr spectrum revealed the presence of 10–15% of the α anomer, which was separated by chromatography. A 6.0-g sample was added to a column (2.5 × 50 cm) of 120 g of silica gel in benzene. The column was eluted with 1.2 l. of benzene–ether (98:2), and the fractions were discarded. An additional 1.2 l. of eluent, gradually changed to benzene–ether (95:5), afforded 4.0 g of the β anomer **6**: $[\alpha]^{23}D$ +25° ($CHCl_3$); nmr τ 2.57–2.80 m (C_6H_5), 5.21 d (1-H), 5.65 q (3-H), 5.90 m (H-4), 6.07 q (SCH_2Ph), 6.40 t (5-H_2), 6.52 s (OCH_3), 7.37 q (2-H), $J_{1,2}$ = 7.5 Hz, $J_{2,3}$ = 3.0, $J_{3,4}$ = 6.8, $J_{4,5a}$ and $J_{4,5b}$ = 2.8 and 3.0 Hz.

Anal. Found: C, 64.9; H, 7.53.

Further elution with benzene–ether (95:5) afforded 0.3 g with a β/α ratio of 3:1. A 0.28-g portion was subjected to preparative tlc on five plates (1-mm thick), developed with benzene–ether (98:2). The faster moving band afforded an additional 163 mg of **6**. The slower band afforded 52 mg of the α anomer: $[\alpha]^{23}D$ −0.6° ($CHCl_3$); nmr τ 2.50–2.82 m (C_6H_5), 5.50 d (1-H), 6.45 q (5-H_2), 6.62 s (OCH_3), 7.08 t (2-H), $J_{1,2}$ = $J_{2,3}$ = 4, $J_{4,5}$ = 3.5 Hz.

Methyl 3,4-*O*-Cyclohexylidene-2-thio-β-D-ribopyranoside (9).—S-Debenzylation of anomerically pure **6** as described below for

(23) J. A. Montgomery and H. J. Thomas, *J. Heterocycl. Chem.*, **1**, 115 (1964).

(24) M. Rasmussen and N. J. Leonard, *J. Amer. Chem. Soc.*, **89**, 5439 (1967).

(25) S. Chladek and J. Smrt *Collect. Czech. Chem. Commun.*, **28**, 1301 (1963).

25 afforded 86% of the thiol, ir 3.89 μ (weak, SH), which was immediately benzoylated.

Methyl 2-*S*-Benzoyl-3,4-*O*-cyclohexylidene-2-thio-β-D-ribopyranoside (10).—The thiol 9 was benzoylated with an equal weight of benzoyl chloride in 10 vol of pyridine. The product was processed as for 26 and crystallized from methanol–water (44% yield), mp 103–106°, after seeding with a sample isolated by preparative tlc in benzene–ether (95:5). A sample for analysis melted at 106–107.5°; $[\alpha]^{22}D$ −126° ($CHCl_3$); nmr (C_6D_6) τ 5.12 d (1-H), 5.60 q (3-H), 5.70 q (2-H), 6.17 pair of triplets (4-H), 6.40 uneven t (5-H_2), 6.80 s (OCH_3), $J_{1,2}$ = 7.6, $J_{2,3}$ = 3.0, $J_{3,4}$ = 7.0, $J_{4,5}$ = 2.5 Hz.

Anal. Calcd for $C_{19}H_{24}O_5S$: C, 62.6; H, 6.64; S, 8.80. Found: C, 62.6; H, 6.76; S, 8.89.

1-*O*-Acetyl-2-*S*-benzyl-3,4-*O*-cyclohexylidene-2-thio-β-D-ribopyranose (8).—To a solution of 5.4 g (13 mmol) of the mesylate in 65 ml of acetic anhydride and 16 ml of acetic acid was added 11 g of potassium acetate. The mixture was heated on a steam bath for 2 hr, cooled, and poured into 800 ml of crushed ice. The product was extracted with chloroform and processed as described below for 17. The yellow oil (5.0 g) showed no mesylate absorption in the ir, but a weak band at 6.22 μ indicated the presence of a little 1,2 olefin. The nmr showed that three products were present, the β-1-*O*-acetate 8 (80%), the anomeric α-1-*O*-acetate (10%), and the 1,2 olefin 7 (10%). A chromatographic column (42 × 2.5 cm) of 100 g of silica gel in benzene, eluted with 750 ml gradually changed from benzene to benzene–ether (99:1), afforded 0.40 g (9.4%) of the olefin **7**, **2-*S*-benzyl-3,4-*O*-cyclohexylidene-2-thio-D-arabinal**: $[\alpha]^{20}D$ +125° ($CHCl_3$); ir 6.22 μ (strong, trans S–C=C–O); nmr τ 2.72 s (C_6H_5), 3.42 s (1-H), 5.52 d (tentatively, 3-H, $J_{3,4}$ = 5.5 Hz), 6.1 s (SCH_2Ph), 5.55–6.65 m (4-H, 5-H_2).

Anal. Calcd for $C_{18}H_{22}O_3S$: C, 67.9; H, 6.96; S, 10.07. Found: C, 67.8; H, 6.86; S, 9.82.

Continued elution with 1.5 ml of benzene–ether, gradually changed from 98:2–96:4, afforded 2.4 g of the 1-*O*-acetate. The β anomer 8 crystallized from 20 ml of methanol: 1.95 g (40%); mp 85–87°; $[\alpha]^{20}D$ −22° ($CHCl_3$); nmr τ 2.66 s (C_6H_5), 3.82 d (1-H), 5.52 q (3-H), 5.80 doublet of triplets (4-H), 6.09 s (SCH_2Ph), 6.30 d (5-H_2), 7.22 q (2-H), 7.90 s (OAc), $J_{1,2}$ = 8.2, $J_{2,3}$ = 2.6, $J_{3,4}$ = 7.1, $J_{4,5}$ = 2.3 Hz.

Anal. Calcd for $C_{20}H_{26}O_5S$: C, 63.5; H, 6.92; S, 8.47. Found: C, 63.6; H, 6.95; S, 8.44.

B. Furanose Series, *S*-Benzyl. 3,5-Di-*O*-benzoyl-D-arabinofuranosyl Chloride (12).—A suspension of 42 g (91 mmol) of 1,3,5-tri-*O*-benzoyl-β-D-arabinofuranose[13] (11) in 1 l. of anhydrous ether was saturated at 0° with anhydrous hydrogen chloride. With exclusion of moisture, the solution was kept at 0° for 3 days, treated again with hydrogen chloride and kept at 0° for 24 hr, treated a third time, stored overnight, and evaporated to dryness. The residue was dissolved in 200 ml of dichloromethane, and the solution was washed with 500 ml of saturated, ice-cold bicarbonate solution, dried, and evaporated to dryness *in vacuo*. The residual oil (35 g) was used without delay.

Benzyl 3,5-Di-*O*-benzoyl-1-thio-α-D-arabinofuranoside (13).—Sodium benzyl mercaptide was prepared by adding 5.0 ml (39 mmol) of α-toluenethiol to a solution of 1.8 g (33 mmol) of sodium methoxide in 50 ml of anhydrous methanol and evaporating to dryness at 60–70° *in vacuo*. To the white residue suspended in 30 ml of anhydrous THF was added, while chilling in ice, a solution of 3,5-di-*O*-benzoyl-D-arabinofuranosyl chloride (32 mmol, based on 11) in 100 ml of anhydrous THF. The mixture was stirred in the ice bath for 40 min and at room temperature for 20 min and then was neutralized with 2.05 g of acetic acid and concentrated. The residue was dissolved in 100 ml of ether and washed with 200 ml of bicarbonate solution and with 200 ml of water and was dried and concentrated. The residual yellow oil (15.8 g) was dissolved in 40 ml of methanol. The solution, seeded with 13 and stored at −5° for 8 days, afforded 4.1 g (28%): mp 102–104°; ir 2.88 (OH), 5.83 (C=O, normal OBz), 5.93 μ (C=O, H-bonded OBz); nmr τ 4.72 d (1-H), 4.83 m (3-H), 5.66 t (2-H), 6.13 d (SCH_2Ph), $J_{1,2}$ = 2.7, $J_{2,3}$ = 2.8 Hz.

In another experiment a sample for analysis was purified by column chromatography on silica gel; dibenzyl disulfide was first eluted with benzene, and 13 was eluted with benzene–ether (95:5) and recrystallized from methanol, mp 103.5–105°, $[\alpha]^{23}D$ +249° ($CHCl_3$).

Anal. Calcd for $C_{26}H_{24}O_6S$: C, 67.2; H, 5.21; S, 6.90. Found: C, 67.3; H, 5.21; S, 7.20.

Benzyl 3,5-Di-*O*-benzoyl-2-*O*-methanesulfonyl-1-thio-α-D-arabinofuranoside (15).—A solution of 0.65 g (1.4 mmol) of crystalline 13 in 10 ml of dry pyridine was chilled in ice, stirred, treated with 0.65 ml of methanesulfonyl chloride, and stored at −5° for 18 hr. The solution was hydrolyzed with 2 ml of water added in drops every 2–3 min, while stirring at ice temperature. Chloroform (30 ml) was added, and the solution was washed with 50 ml of bicarbonate solution and with 50 ml of water and was dried and concentrated without heating. The residue (0.80 g, 105%) traveled as a single spot on tlc in benzene–ether (90:10) when detected by both ultraviolet light and charring with sulfuric acid spray: nmr τ 4.45 broad s (1-H, 2-H), 4.79 t (3-H), 5.29 broad s (4-H, 5-H_2), 6.11 s (SCH_2Ph), 7.01 s (OSO_2CH_3), $J_{2,3}$ = $J_{3,4}$ = 1.5 Hz; $[\alpha]D$ +108° ($CHCl_3$). The compound decomposed on attempted chromatographic purification but could be stored for 1 week with little decomposition (darkening, appearance of slight OH absorption in the infrared). There was no decomposition under the conditions of its formation; a sample in pyridine-d_5 solution was stored overnight with no change in the nmr spectrum.

1-*O*-Acetyl-3,5-di-*O*-benzoyl-2-*S*-benzyl-2-thio-α,β-D-ribofuranoside (17).—To 0.68 g (1.3 mmol) of mesylate 15 was added 2 ml of glacial acetic acid, 8 ml of acetic anhydride, and 0.9 g of potassium acetate. The mixture was heated on a steam bath for 2 hr, cooled, and poured into 50 ml of ice water and stirred for 30 min. The product was extracted with two 30-ml portions of chloroform. The extracts were washed with two 50-ml portions of bicarbonate solution (foaming) and with 50 ml of water, dried, and concentrated. (Any remaining acetic anhydride was destroyed by treatment with 2 ml of pyridine and 10 ml of methanol, concentration, and partition of the residue between chloroform and bicarbonate as before.) The yield of residual product was 0.58 g (90%), $[\alpha]^{24}D$ −3.7° ($CHCl_3$). In different runs the anomeric ratio, $\beta:\alpha$, varied from 60:40 to 70:30 according to the nmr spectrum: nmr for β, τ 2.79 s (C_6H_5 of benzyl), 3.63 d (1-H), 4.32 q (3-H), 6.20 s (SCH_2Ph), 6.25 q (2-H), 8.10 s (OAc), $J_{1,2}$ = 2.5, $J_{2,3}$ = 6.8, $J_{3,4}$ = 4.6 Hz; nmr for α, τ 2.77 s (C_6H_5 of benzyl), 3.54 d (1-H), 4.36 q (3-H), 6.25 s (SCH_2Ph), 6.55 q (2-H), 7.88 s (OAc), $J_{1,2}$ = 4.5, $J_{2,3}$ = 6.8, $J_{3,4}$ = 1.5 Hz.

3,5-Di-*O*-benzoyl-2-*S*-benzyl-2-thio-D-ribofuranosyl chloride (20) was prepared from the oily α,β-1-*O*-acetate 17, as described below for 22, held under vacuum 2 hr, and then used immediately.

6-Chloro-9-(2-*S*-benzyl-3,5-di-*O*-benzoyl-2-thio-α,β-D-ribofuranosyl)-9*H*-purine (9-27).—To 385 mg (0.760 mmol) of α,β-1-*O*-acetate 17 was added 148 mg (0.970 mmol) of 6-chloropurine (90% pure, from ultraviolet extinctions) and 5 mg of chloroacetic acid. The materials were intimately mixed, forming a gum, and were fused under vacuum by immersion in a bath at 172–175° for 90 sec. The cooled residue was dissolved in 5 ml of chloroform. On chilling, the solution deposited 57 mg of unreacted 6-chloropurine (assume 91 mg reacted, 78%). Concentration of the filtrate afforded 460 mg of a dark oil. The nmr spectrum disclosed the presence of unreacted 1-acetate 17, 5-(benzoyloxymethyl)-2-(*S*-benzyl)furan-2-thiol (**34a**), and nucleoside **27**, in the ratio 5:54:41.

The nucleoside fraction was isolated by preparative tlc of the residue on two plates (2-mm thick), developed with $CHCl_3$–MeOH (98:2), dried, and developed again. The band, R_f 0.8–0.9, contained sugar and the furan. The band, R_f 0.5, was eluted with $CHCl_3$–MeOH (9:1) to yield 120 mg (38%) of nucleoside. The anomeric ratio $\beta:\alpha$ was 2:1 by nmr analysis. A solution in 5 ml of methanol chilled to −10° afforded 18 mg, mp 148–160°, recrystallized again from 2 ml to give 14 mg (4%) of α-**9-27**: mp 160–163°; ir 5.78, 5.83 (C=O), 6.30, 6.39 μ (purine aryl); nmr 1.23 s and 1.49 s (H-2, H-8), 2.82 s (C_6H_5 of benzyl), 3.18 d (1-H), 4.33 q (3-H), 5.95 t (2-H), 6.32 s (SCH_2Ph), $J_{1,2}$ = 7.0, $J_{2,3}$ = 6.5, $J_{3,4}$ = 1.6, $J_{4,5}$ = 4.5 Hz.

The mother liquor residue was enriched in β-**9-27**. From another experiment the $\beta:\alpha$ ratio was now 4:1: nmr β, for τ 1.52 s and 1.89 s (H-2, H-8), 3.03 s (C_6H_5 of benzyl), 3.84 d (1-H), 4.14 q (3-H), 5.51 q (2-H), 6.42 s (SCH_2Ph), $J_{1,2}$ = 9.0, $J_{2,3}$ = 6.0, $J_{3,4}$ = 1.8 Hz.

5-(Benzoyloxymethyl)-2-*S*-benzylfuran-2-thiol (34a).—In one experiment the preparative tlc plates (from 9-27, above) were developed first with benzene to separate this elimination product, R_f 0.9, from the 1-acetate 17, R_f 0.8 (the nucleoside had R_f 0.05 in this system). Elution with chloroform afforded a yellow oil, which darkened on standing: ir 5.82, 7.90, 14.1 (strong, OBz), 6.28, 6.35 (aryl), 6.70, 6.90 μ (benzyl); nmr τ 1.8–2.1 and 2.4–2.7

(OBz), 1-H obscured but possibly at 2.51 s, 2.77 s (C_6H_5 of benzyl), 3.65 s (3-H), 4.79 s (5-H_2), 6.15 s (SCH_2Ph).

6-Benzamido-9(7)-(2-*S*-benzyl-3,5-di-*O*-benzoyl-2-thio-α,β-D-ribofuranosyl)-9*H*(7*H*)-purine (28). I.—To a solution of 0.90 g (1.8 mmol) of chloro sugar **20** in 10 ml of dichloromethane (dried over molecular sieve) was added 0.45 g (1.9 mmol) of 6-benzamidopurine and 3 g of molecular sieve (4A, 1/16-in. diam). The mixture was protected from moisture, stirred at room temperature for 7 days, and filtered through Celite. The filter cake was washed with two 25-ml portions of dichloromethane. Concentration of the combined filtrates afforded 0.8 g (65%) of an oil. Preparative tlc on four plates (2-mm thick) developed twice with $CHCl_3$–MeOH (98:2) afforded a nucleoside band, R_f 0.5, which was eluted to give 70 mg (6%): ir 5.79 (C=O), 6.12, 6.32 μ (purine aryl). The nmr spectrum showed it was mainly α-**9-28** (α:β ratio 9:1): nmr for α, τ 1.21 s and 1.61 s (H-2, H-8), 2.83 s (C_6H_5 of benzyl), 3.10 d (1′-H), 4.37 q (3′-H), 5.95 t (2′-H), 6.32 s (SCH_2Ph), $J_{1,2}$ = 7.0, $J_{2',3'}$ = 6.8, $J_{3',4'}$ = 1.5, $J_{4',5'}$ = 4.2 Hz.

II.—A mixture of chloro sugar **20** (22 mmol, based on 1-acetate **17**), 13 g (37 mmol) of freshly distilled bis(trimethylsilyl)-6-benzamidopurine,[26,27] and 8.3 g (23 mmol) of mercuric bromide in 250 ml of dry benzene was stirred. After 1 min, the cloudy mixture became clear. The solution was stirred for 6 days at room temperature and evaporated. The residue was slurried with 250 ml of chloroform–methanol (4:1) and the mixture filtered through Celite to remove 6-benzamidopurine. The filtrate was evaporated and the residue redissolved in 200 ml of chloroform. The solution was washed with 100 ml of aqueous 30% potassium iodide and with 300 ml of water, dried, and concentrated. The residual foamed glass, 18 g, showed ir absorption bands for both **9-28** and **7-28**; tlc in $CHCl_3$–MeOH (95:5) showed nucleoside spots at R_f 0.7 (**9-28**) and R_f 0.5 (**7-28**) in addition to contaminants at the solvent front (sugar derivatives) and origin (6-benzamidopurine).

The crude product was chromatographed on a column (37 × 4.5 cm) of 200 g of silica gel in benzene. Elution with 2.5 l. of benzene afforded sugar impurities in a first fraction which was discarded. Additional 1.5 l. of benzene afforded 2.8 g (18%) of nucleoside, identified as **9-28** (with a β:α ratio of 4:1, by nmr), containing a little 7 isomer, by infrared analysis and tlc. Finally, elution with 1.2 l. of benzene gave another 2.8 g (total yield 5.6 g, 37%) of nucleoside consisting of 9 and 7 isomers in nearly equal amounts, from the ir spectrum and tlc.

The mixture was separated by preparative tlc of this latter fraction on 12 plates (2-mm thick), each developed four times with $CHCl_3$–MeOH (98:2). Elution of the faster band with $CHCl_3$–MeOH (95:5) afforded 0.9 g of 9 isomer, as a glass, characterized by the uv spectrum and by normal ir bands at 6.22 and 6.31 μ (medium, purine aryl) in addition to strong benzoate bands. The nmr spectrum showed it was mainly β-**9-28**, with a β:α ratio of 85:15: for β, τ 1.45 s (2-H or H-8; another singlet was obscured by the aryl H's perhaps at 2.85), 2.97 s (C_6H_5 of benzyl), 3.78 d (1′-H), 4.23 q (3′-H), 6.45 s (SCH_2Ph), $J_{1',2'}$ = 9.0, $J_{2',3'}$ = 6.5 Hz, $J_{3',4'}$ = 1.5 Hz.

In another experiment a sample for analysis was obtained by preparative tlc directly on the crude product.

Anal.[28] Calcd for $C_{38}H_{31}N_5O_6S$: C, 66.6; H, 4.56; N, 10.2; S, 4.67. Found: C, 63.10; H, 4.36; N, 9.72; S, 4.77.

Elution of the slower band from the plates afforded 1.2 g of **7-28**, as a glass, characterized by uv and by unexpected ir bands at 6.08 and 7.58 (strong), 6.23 and 6.40 (medium), in addition to benzoate bands at 5.78, 7.85, and 14.05 μ. The anomeric composition could not be determined from the nmr.

Anal.[28] Found: C, 64.9; H, 4.32; N, 9.99.

9-(2-*S*-Benzyl-2-thio-α,β-D-ribofuranosyl)-9*H*-adenine (9-31). I. **From β(α)-9-27.**—A solution of 0.41 g (0.67 mmol) of **9-27** (isolated by preparative tlc, and with β:α ratio of 4:1 after some α-**9-27** was separated by crystallization) in 15 ml of methanol was saturated at 5° with anhydrous ammonia, heated in a steel bomb at 100° for 15 hr, and concentrated. The residue was triturated with two 20-ml portions of ether (to remove methyl benzoate) and then with 10 ml of hot chloroform. Somewhat surprisingly the nucleoside dissolved; insoluble ammonium chloride was left. The residue obtained on evaporation of the chloroform showed two components by tlc in $CHCl_3$–MeOH (3:1), R_f 0.8 and 0.9. These were separated by preparative tlc on two plates (2-mm thick) developed with $CHCl_3$–MeOH (82:18). Eluted with $CHCl_3$–MeOH (7:3), the faster band afforded 170 mg of β-**9-31** contaminated with benzamide. Crystallization from 2 ml of acetone gave 35 mg (14%), mp 114–120°; recrystallization yielded 31 mg, dried at 60° (1 mm), mp 156–158°. Acetone of solvation was observed in the ir and nmr spectra and elemental analysis: ir 5.86 (acetone C=O), 6.03 (strong, NH_2), 6.28 μ (strong, purine aryl); nmr, in acetone-d_6 exchanged with D_2O, τ 1.80 s and 1.83 s (2-H, 8-H), 2.97 m (C_6H_5), 3.97 d (1′-H), 5.45 q (3′-H), 5.7 q (4′-H), 6.18 d (5′-H_2), 6.05 q (2′-H), 6.43 d (SCH_2Ph, J = 1 Hz), $J_{1',2'}$ = 9.3, $J_{2',3'}$ = 5.0, $J_{3',4'}$ = 1.0, $J_{4',5'}$ = 2.5 Hz.

Anal. Calcd for $C_{14}H_{13}N_5O_2S \cdot C_3H_6O$: C, 55.8; H, 5.39; N, 16.3. Found: C, 55.7; H, 5.84; N, 16.2.

Elution of the slower band afforded 20 mg, crystallized from acetone to give 8 mg of α-**9-31**, mp 100–114°. Further recrystallization (adding material from another experiment) raised the mp to 116–120°, a hydrate even after drying at 60° (1 mm): ir 6.00 (NH_2), 6.22 μ (purine aryl); nmr, in acetone-d_6 exchanged with D_2O, τ 1.60 s and 1.69 s (2-H, 8-H), 2.75 s (C_6H_5), 3.42 d (1′-H), 5.48 q (3′-H), 5.67 m (4′-H), 6.24 d (5′-H_2), 5.85 q (2′-H), 6.20 s (SCH_2Ph), $J_{1',2'}$ = 7.5, $J_{2',3'}$ = 6.0, $J_{3',4'}$ = 2.0, $J_{4',5'}$ = 3.7 Hz.

II. **From β(α)-9-28.**—To a solution of 1.4 g (2.0 mmol) of β-**9-28** (containing 15% of α-**9-28**) in 20 ml of methanol was added 4 ml of 1 *N* sodium methoxide in methanol. The solution was refluxed for 2 hr. The dark solution was cooled, neutralized with 4 ml of 1 *N* acetic acid in methanol, and evaporated to dryness. The residue was triturated with two 30-ml portions of hot cyclohexane. The insoluble residue was dissolved in 30 ml of hot acetone and filtered. The filtrate was reduced in volume to 15 ml and chilled to give 395 mg (50%) of β-**9-31**, dried at 100° (1 mm), mp 153–155°; nmr same as β-**9-31** from I.

7-(2-*S*-Benzyl-2-thio-D-ribofuranosyl)-7*H*-adenine (7-31).—A solution of 0.70 g (1.0 mmol) of **7-28** in 50 ml of anhydrous methanol was treated with 0.10 g (1.8 mmol) of sodium methoxide, refluxed for 3 hr, cooled, and neutralized with about 3 ml of IRC 50 resin (H), which was then removed on a filter. The filtrate was concentrated and the residue was triturated with cyclohexane to remove methyl benzoate. The solid was collected on a filter: 0.24 g; tlc in $CHCl_3$–MeOH (8:2) showed two spots, R_f 0.6 and 0.8.

Preparative tlc on four plates (2-mm thick), developed and eluted with the above solvent, afforded **7-31** from the slower band; it was crystallized from ethanol to give 44 mg (9%): mp 211–216°; ir 6.05 and 6.23 (strong), 6.41 and 6.58 μ (medium).

Anal. Calcd for $C_{17}H_{19}N_5O_3S$: C, 54.7; H, 5.13; N, 18.8; S, 8.58. Found: C, 54.5; H, 5.11; N, 18.9; S, 8.69.

The faster band afforded **6-benzamido-7-(2-*S*-benzyl-2-thio-D-ribofuranosyl)-7*H*-purine (7-32)** which was crystallized from ethanol–water (2:1), giving 95 mg (20%): mp 110–115°; ir 6.10 (strong), 6.27 and 6.40 μ (medium). The anomeric composition could not be determined from the nmr.

Anal. Calcd for $C_{24}H_{23}N_5O_4S$: C, 60.4; H, 4.86; N, 14.7; S, 6.71. Found: C, 60.2; H, 4.75; N, 14.6; S, 6.33.

C. *S*-Benzoyl Series. Methyl 3,5-Di-*O*-benzoyl-2-*S*-benzyl-2-thio-α,β-D-ribofuranoside (23).—To 5.2 g (9.6 mmol) of mesylate **15** in 500 ml of anhydrous methanol was added 7 g of Drierite ($CaSO_4$ drying agent) and 6.0 g (22 mmol) of silver carbonate. The mixture, protected from moisture and light, was refluxed for 18 hr and then filtered through Celite. The Celite was washed with 100 ml of chloroform, and the combined filtrate was concentrated. The residue in 50 ml of chloroform solution was washed with 200 ml of 2 *M* ammonium hydroxide and with 100 ml of water, dried, and concentrated. To remove silver salts from the dark residual oil (4.6 g), a second washing with ammonium hydroxide of a chloroform solution was required, followed by filtration of a benzene solution through Celite. The yellow oil (4.2 g, 92%) was a mixture of anomers (β:α ratio 3:2): nmr for β-**23**, τ 2.68 s (C_6H_5 of benzyl), 4.38 q (3-H), 4.98 d (1-H), 6.19 s (SCH_2Ph), 6.40 q (H-2), 6.63 s (OCH_3), $J_{1,2}$ = 3.2, $J_{2,3}$ = 6.5, $J_{3,4}$ = 4.2 Hz; nmr for α-**23**, τ 2.68 s (C_6H_5 of benzyl), 4.58 q (3-H), 5.10 d (1-H), 6.27 s (SCH_2Ph), 6.58 s (OCH_3), 6.73 q (2-H), $J_{1,2}$ = 4.8, $J_{2,3}$ = 7.1, $J_{3,4}$ = 2.5 Hz.

Methyl 2-*S*-Benzyl-2-thio-α,β-D-ribofuranoside (24).—To 4.2 g

(26) T. Nishimura and I. Iwai, *Chem. Pharm. Bull.*, **12**, 352 (1964).

(27) I. Iwai, T. Nishimura, and B. Shimizu in "Synthetic Procedures in Nucleic Acid Chemistry," Vol. I., W. W. Zorbach and R. S. Tipson, Ed., Interscience, New York, N. Y., 1968, p 135.

(28) Low values for carbon suggested a little solvent was retained in the glass, but an acceptable nitrogen (and sulfur) composition of the nucleoside was determined.

(8.6 mmol) of the dibenzoate **23** in 500 ml of 50% aqueous methanol was added 9 g of potassium hydroxide, and the mixture was refluxed for 2 hr, neutralized with CO_2, and concentrated. The semisolid residue was dissolved in 30 ml of water, and the product was extracted with two 50-ml portions of chloroform. The extracts were washed with 50 ml of water, dried, and concentrated. The yellow oil weighed 2.2 g (95%): nmr τ, for β, 5.16 d (1-H), 5.82 q (3-H), 6.22 s (SCH_2Ph), 6.65 s (OCH_3), 6.72 q (2-H), $J_{1,2}$ = 3.4, $J_{2,3}$ = 5.6, $J_{3,4}$ = 3.4 Hz; nmr τ, for α, 5.17 d (1-H), 6.08 q (3-H), 6.30 s (SCH_2Ph), 6.59 s (OCH_3), 6.88 q (2-H), $J_{1,2}$ = 5.0, $J_{2,3}$ = 6.4, $J_{3,4}$ = 2.5 Hz; nmr for both, 2.70 s (C_6H_5 of benzyl).

Anal. Calcd for $C_{13}H_{18}O_4S \cdot 0.04CHCl_3$: C, 56.9; H, 6.61; S, 11.7; Cl, 1.55. Found: C, 56.8; H, 6.75; S, 11.9; Cl, 0.37.

Methyl 2-Thio-α,β-D-ribofuranoside (25).—A solution of 3.5 g (13 mmol) of 2-benzylthio compound **24** in 15 ml of anhydrous 1,2-dimethoxyethane was added dropwise to a solution of 2.0 g (90 mmol) of sodium in 100 ml of liquid ammonia under a Dry Ice–acetone condenser, excluding moisture. The mixture was stirred at reflux for 1 hr, retaining the blue color. (If insufficient sodium was used, the solution turned yellow. In the absence of 1,2-dimethoxyethane as cosolvent, the reaction failed to go to completion.) The excess sodium was decomposed by adding 5 g of ammonium chloride, and the ammonia was evaporated under a stream of nitrogen. Water (15 ml) was added to the residue. The solution was neutralized to pH 6–7 with acetic acid and was extracted with ten 30-ml portions of chloroform. The combined extracts were dried and concentrated to a yellow oil: 1.1 g (50%); ir 3.9 μ (weak, SH); nmr τ 5.04 d (1-H of α, $J_{1,2}$ = 5.0 Hz), 5.09 d (1-H of β, $J_{1,2}$ = 2.8 Hz), 6.52 s (OCH_3, both kinds); the β:α ratio was 3:2. An additional 0.7 g (total yield 80%) was obtained by continuous extraction of the water layer with chloroform overnight. Each fraction was benzoylated immediately.

Methyl 2-*S*-Benzoyl-3,5-di-*O*-benzoyl-2-thio-α,β-D-ribofuranoside (26).—To 1.1 g (6.1 mmol) of the thiol **25** in 20 ml of dry pyridine was added, with stirring and ice cooling, 3.0 ml (26 mmol) of benzoyl chloride. The mixture was stirred at room temperature overnight, chilled, and treated with 1 ml of water dropwise to hydrolyze the excess benzoyl chloride. It was then diluted with 50 ml of bicarbonate solution and extracted with 50 ml of chloroform. The extract was washed with 50 ml of water, dried, and concentrated to an oil, 2.7 g (90%). The ratio β:α was 62:38 by nmr analysis: τ for β, 3.98 m (3-H), 4.80 d (1-H, $J_{1,2}$ = 2.5 Hz), 6.51 s (OCH_3); τ for α, 4.22 q (3-H, $J_{2,3}$ = 7, $J_{3,4}$ = 2 Hz), 4.70 d (1-H, $J_{1,2}$ = 4.5 Hz), 6.49 s (OCH_3).

Acetyl 2-*S*-Benzoyl-3,5-di-*O*-benzoyl-2-thio-α,β-D-ribofuranose (18).—A solution of 3.8 g (7.7 mmol) of **26** in 50 ml of acetic anhydride and 10 ml of acetic acid was chilled to −20° and treated, while stirring, with 0.4 ml of concentrated sulfuric acid. The solution was stored overnight at −20° (to avoid freezing at a lower temperature) and poured into 50 ml of ice water. The mixture was stirred for 30 min and extracted with two 30-ml portions of chloroform. The extracts were washed with 50 ml of bicarbonate solution, dried, and concentrated. The residual oil, according to the infrared spectrum, retained a little acetic anhydride, which was decomposed by adding 1 ml of pyridine and 15 ml of methanol and evaporating the solution. The oil was partitioned again with 30 ml of chloroform and 50 ml of bicarbonate solution, washed with 30 ml of water, and recovered, 3.9 g (97%). The nmr spectrum showed no OMe signal; the β:α ratio varied from 2:3 to 1:6 in different runs: nmr τ, for β, 3.49 d (1-H), 3.98 q (3-H), 5.09 q (2-H), 8.00 s (OAc), $J_{1,2}$ = 3.0, $J_{2,3}$ = 6.3, $J_{3,4}$ = 1.4 Hz; for α, 3.28 d (1-H), 4.15 q (3-H), 5.09 q (2-H), 7.81 s (OAc), $J_{1,2}$ = 4.7, $J_{2,3}$ = 6.7, $J_{3,4}$ = 1.5 Hz.

2-*S*-Benzoyl-3,5-di-*O*-benzoyl-2-thio-D-ribofuranosyl chloride (21) was prepared in quantitative yield from the α,β-1-*O*-acetate **18** as described for **22**, held under vacuum for 2 hr, and used immediately.

6-Benzamido-9-(2-*S*-benzoyl-3,5-di-*O*-benzoyl-2-thio-β-D-ribofuranosyl)-9*H*-purine (β-9-29).—A mixture of 3.7 g (7.5 mmol, based on α,β-1-*O*-acetate **19**) of chloro sugar **21**, 4.0 g (10 mmol) of bis(trimethylsilyl)-6-benzamidopurine,[26,27] 3.0 g (8.3 mmol) of mercuric bromide, and 150 ml of dry benzene was stirred. It became clear after a few minutes and was stirred at room temperature for 3 days and then at reflux for 2 days to isomerize most of the **7-29** to **β-9-29**. The solution was concentrated, and the residue was dissolved in 50 ml of chloroform and filtered through Celite to remove 6-benzamidopurine. The filtrate was washed with 50 ml of aqueous 30% potassium iodide and with 50 ml of water, dried, and concentrated. The residue (4.0 g) was analyzed by tlc in chloroform–ethyl acetate (2:1); it contained a little sugar impurity, R_f 0.8; mostly **β-9-29**, R_f 0.6; some **7-29**, R_f 0.4; and a little 6-benzamidopurine, R_f 0.0.

The product was chromatographed on a column (40 × 2.5 cm) of 80 g of silica gel in benzene. Elution with 1 l. gradually changed from benzene to benzene–ethyl acetate (9:1) afforded 0.64 g of benzoic acid and an elimination product, presumably **34b**, characterized by its spectra: ir 5.80, 7.86, 14.02 (OBz), 5.92, 8.28, 11.10, 14.58 μ (SBz); nmr τ 1.71–2.25 and 2.35–2.90 m (C_6H_5 of benzoyl), 2.35 s (1-H), 3.36 s (3-H), 4.64 s (5-H_2).

Additional 3.5 l. of eluent, gradually changed from benzene–ethyl acetate 9:1 to 8:2, afforded 1.92 g of nucleoside; the presence of a little 7 isomer could be seen in the ir. The nucleoside mixture was resolved by preparative tlc on ten plates (2-mm thick) and developed twice with $CHCl_3$–MeOH (98:2). Elution of the faster band with $CHCl_3$–MeOH (90:10) afforded 1.3 g (25%) of **β-9-29** as a foamed glass. In addition to strong OBz bands in the ir at 5.80, 7.9, 14.05 μ and medium SBz bands at 5.97, 8.25, 11.03, and 14.53 μ, purine ring bands at 6.22 and 6.32 μ (medium) were characteristic for the 9 isomer: nmr τ 1.28 s and 1.70 s (2-H and 8-H), 3.38 d (1′-H), 3.95 (3′-H), 4.51 (2′-H), $J_{1',2'}$ = 9.0, $J_{2',3'}$ = 5.8, $J_{3',4'}$ = 1.4 Hz. No signals attributable to the α anomer could be detected.

Anal. Calcd for $C_{38}H_{29}N_5O_7S \cdot {}^1/_2H_2O$: C, 64.4; H, 4.27; N, 9.88; S, 4.52. Found: C, 64.5; H, 4.27; N, 9.84; S, 4.13.

6-Benzamido-7-(2-*S*-benzoyl-3,5-di-*O*-benzoyl-2-thio-D-ribofuranosyl)-7*H*-purine (7-29).—From another experiment in which the reaction mixture was not heated before work-up, the ratio of **9-29** to **7-29** was 5:2, isolated by preparative tlc. Elution of the slower moving band afforded 10 mg of **7-29**, identified by the uv (Table III) and ir spectra; in addition to strong OBz bands, medium SBz bands, and the usual purine ring band at 6.22 μ (medium), bands at 6.08 (strong) and 6.38 (medium) and a minimum at 6.29 μ were characteristic for the 7-nucleoside.

Alkaline Methanolysis of β-9-29.—A solution of 0.50 g (1.0 mmol) of **β-9-29** in 20 ml of methanol was treated with 130 mg of sodium methoxide, refluxed for 2 hr, and neutralized with 145 mg of glacial acetic acid. The solution was evaporated, and the residue was partitioned between 5 ml of water and 5 ml of chloroform. A solid at the interface was removed on a filter and identified as 37 mg (27%) of adenine. Evaporation of the chloroform afforded methyl benzoate. The residue obtained by evaporating the water layer contained additional adenine, by tlc analysis. For isolation of any sugar derivatives, the residue was acetylated with 2 ml of acetic anhydride in 10 ml of pyridine. The mixture was stirred overnight at room temperature, treated with 5 ml of methanol to decompose excess anhydride, and evaporated. The residue was dissolved in 20 ml of chloroform, and the solution was washed with 30 ml of water, dried, and evaporated. The residual oil (150 mg, 57%) without purification was identified as the disulfide **35** of **methyl 3,5-di-*O*-acetyl-2-thio-β-D-ribofuranose** by nmr and mass spectral (*m/e*, parent peak 526) analysis: nmr τ 4.67 q (3-H), 4.96 d (1-H), 6.32 q (2-H), 6.60 s (OCH_3), 7.88 s and 7.90 s (two OAc's), $J_{1,2}$ = 2.3, $J_{2,3}$ = 6.5, $J_{3,4}$ = 4.0 Hz.

D. 7-Isoadenosine. 6-Benzamido-7-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-7*H*-purine (37).—A stirred solution of 15 g (29 mmol) of 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in 200 ml of dry benzene was treated with 40 mmol of bis(trimethylsilyl)-6-benzamidopurine[26,27] and 10 g (29 mmol) of mercuric bromide. After 3 days at room temperature, the mixture was evaporated, and the residue was slurried with 100 ml of aqueous 30% potassium iodide and 150 ml of chloroform. The mixture was filtered. The chloroform layer was separated, washed with 100 ml of water, dried, and evaporated. The residue (15 g) showed two strong spots on tlc in $CHCl_3$–MeOH (50:1), R_f 0.15 and 0.35, plus sugar by-product at the solvent front and 6-benzamidopurine at the origin.

Initially in a small experiment, the two major components were separated by preparative tlc. The faster traveling component (14%) was identified as a 6-benzamido-9-(2,3,5-tri-*O*-benzoyl-D-ribofuranosyl)-9*H*-purine by the uv spectrum (Table III), and as the β anomer **36**[20] on debenzoylation with methanolic sodium methoxide to give adenosine. The slower component crystallized from methanol (11%), mp 120–124°, and was of analytical purity. The uv (Table III) and ir spectra suggested it was a 7 isomer, presumably the β anomer[20] **37**: ir 6.10 (strong), 6.27 and 6.40 μ (medium), in addition to strong benzoate bands; absence of bands for 6-benzamidopurine could be observed at 5.91 μ and, for large amounts, at 6.42 and 6.59 μ. On seeding with these crystals, the crude residue from the larger run above, in 300 ml

of methanol solution, afforded 1.0 g (5.5%) of **37**, mp 116–123°. The compound was previously[20] described as amorphous and shown to be the β anomer.

Anal. Calcd for $C_{38}H_{29}N_5O_8$: C, 66.8; H, 4.28; N, 10.2. Found: C, 66.6; H, 4.41; N, 10.2.

7-β-D-Ribofuranosyladenine (39) and the 6-*N*-Benzoyl Derivative 38.—A solution of 0.53 g (0.78 mmol) of tetrabenzoyl compound **37** in 30 ml of methanol was treated with 108 mg (2.00 mmol) of sodium methoxide, refluxed for 1.5 hr, neutralized with 3 ml of IRC 50 (H) resin, filtered, and concentrated. The residue was triturated with 40 ml of hot cyclohexane to remove methyl benzoate, and 210 mg of brown solid was collected on a filter: tlc in $CHCl_3$–MeOH (3:1) showed three spots, R_f 0.4, R_f 0.6, and R_f 0.9. Preparative tlc on three plates (2-mm thick), each developed three times with $CHCl_3$–MeOH (4:1), afforded additional methyl benzoate from the band at R_f 0.9. The middle band, R_f 0.6, was eluted with chloroform–methanol (6:4) to give 50 mg of 6-benzamido-7-β-D-ribofuranosylpurine (**38**); crystallization from methanol afforded 36 mg (12%): mp 155–160°; ir 6.12 (strong), 6.30 (medium), 6.65 μ (strong). Presence of the 6-*N*-benzoyl group and facile acid cleavage to 6-benzamidopurine was demonstrated in the ultraviolet spectra (Table III).

Anal. Calcd for $C_{17}H_{17}N_5O_5 \cdot {}^1/_2H_2O$: C, 53.7; H, 4.77; N, 18.4. Found: C, 53.9; H, 4.59; N, 18.4.

Elution of the slow band afforded 10 mg (5%) of 7-β-D-ribofuranosyladenine; ir 6.09 (strong), 6.27 (medium), 6.39 μ (weak). In the uv spectrum (Table III), the difference $\lambda_{min}^{pH\ 1} - \lambda_{min}^{pH\ 7} = +8$ mμ was that of a 7-ribofuranosyladenine, as distinguished[21,22] from that of 3-β-D-ribofuranosyladenine (−8 mμ).

E. *S*-Methyl Series. Methyl 3,5-Di-*O*-benzoyl-1-thio-α-D-arabinofuranoside (14).—To 100 g (2.04 mol) of methanethiol in a flask cooled in ice and equipped with a Dry Ice condenser and a drying tube was added 7.0 g of 58% sodium hydride in mineral oil (0.17 mol). The mixture was stirred at reflux for 2 hr. To this was added gradually, with foaming, a solution of 3,5-di-*O*-benzoyl-D-arabinofuranosyl chloride (**12**, obtained from 42 g of **11**, 91 mmol) in 100 ml of anhydrous THF. The mixture was stirred at room temperature under the Dry Ice condenser for 0.5 hr and poured onto a mixture of 100 ml of ice and 500 ml of bicarbonate solution. The solid that formed dissolved on dilution to 2 l. with water. The solution was extracted with three 250-ml portions of dichloromethane. The combined extracts were washed with 700 ml of saturated salt solution, dried, and concentrated. The residual crude product was used without purification. Signals in the nmr at τ 4.66 d (1-H, $J_{1,2}$ = 2.4 Hz), 5.60 t (2-H, $J_{2,3}$ = 2.8 Hz), 7.80 s (SCH_3) were identified by comparison with a previous sample isolated chromatographically.

Methyl 3,5-Di-*O*-benzoyl-2-*O*-methanesulfonyl-1-thio-α-D-arabinofuranoside (16).—Crude **14** in 250 ml of pyridine at −5° was treated gradually with 35 ml of methanesulfonyl chloride. After 18 hr at −5°, the excess chloride was hydrolyzed by treating the solution dropwise with water, while stirring and keeping the temperature below 15°, until (after about 1 hr) no further heat evolution could be detected. The solution was poured into 1 l. of ice water, and the mixture was extracted with three 200-ml portions of dichloromethane. The extracts were washed with 700 ml of sodium bicarbonate and with 700 ml of water, dried, and concentrated. The residue was used without purification: 41 g; nmr τ 4.45 d (1-H), 4.53 q (3-H), 4.83 t (2-H), 6.91 s (OSO_2CH_3), 7.77 s (SCH_3), $J_{1,2}$ = 1.5, $J_{2,3}$ = 1.2, $J_{3,4}$ = 5.0 Hz. Weak, unresolved singlets adjacent to the OSO_2CH_3 and SCH_3 singlets were attributed to a small precentage of the β anomer.

1-*O*-Acetyl-3,5-di-*O*-benzoyl-2-*S*-methyl-2-thio-α,β-D-ribofuranoside (19).—A solution of the mesylate **16** (41 g) in 500 ml of acetic anhydride and 125 ml of acetic acid was treated with 100 g of potassium acetate, heated on the steam bath for 3 hr, cooled, poured into 2 l. of ice water, and stirred for 30 min. The product was isolated by extraction and freed of acetic anhydride as for **17**. The oil (39 g) was purified by chromatography on a column (76 × 5.0 cm) of 90–200 mesh silica gel in benzene. The eluent was gradually changed to benzene–ether (95:5) while 4 l. of eluate was collected. Elution with 5 l. of benzene–ether (95:5) then afforded 23.9 g (61% based on **11**) of 1-acetate. The anomeric ratio, β:α, was 60:40 according to the nmr spectrum: τ, for β, 3.63 d (1-H), 4.25 t (3-H), 6.24 q (2-H), 7.82 s (SCH_3), 8.00 s (OAc), $J_{1,2}$ = 2.0, $J_{2,3}$ = 6.5, $J_{3,4}$ = 5.0 Hz; for α, 3.40 d (1-H), 3.30 q (3-H), 6.52 q (2-H), 8.00 s and 8.02 s (SCH_3 and OAc), $J_{1,2}$ = 4.7, $J_{2,3}$ = 6.4, $J_{3,4}$ = 1.8 Hz.

The β anomer could be isolated by two crystallizations from 95% ethanol to give 6.5 g, mp 87–88°, $[\alpha]^{20}D$ +7.3° ($CHCl_3$). An additional 1.5 g could be crystallized from the adjacent chromatographic fractions.

Anal. Calcd for $C_{22}H_{22}O_7S$: C, 61.4; H, 5.15; S, 7.44. Found: C, 61.4; H, 4.92; S, 7.27.

3,5-Di-*O*-benzoyl-2-*S*-methyl-2-thio-D-ribofuranosyl Chloride (22).—A solution of 8.5 g (20 mmol) of α,β-1-*O*-acetate **19** in 200 ml of anhydrous ether was chilled to −70° with Dry Ice–acetone and saturated with a stream of anhydrous hydrogen chloride. The solution was stored at −70° excluding moisture for 4 days. The resultant clear, purple solution was concentrated on the water aspirator and the residue held under vacuum (1 mm) for 1 hr at room temperature. The oil (8.5 g) was used immediately.

6-Benzamido-9(7)-(3,5-di-*O*-benzoyl-2-*S*-methyl-2-thio-α,β-D-ribofuranosyl)-9-(7*H*)-purine (30).—To a solution of chloro sugar (**22**, based on 20 mmol of **19**) in 225 ml of dry benzene was added, with stirring, 9.9 g (39 mmol) of freshly distilled bis(trimethylsilyl)-6-benzamidopurine[26,27] and 8.0 g (22 mmol) of mercuric bromide. The mixture became clear after 10 min, and stirring was continued at room temperature for 3 days. The solution was concentrated and the residue was partitioned between 250 ml of chloroform and 250 ml of water. Some unreacted 6-benzamidopurine separated as a fine solid at the interface and was removed by filtration of both layers through Celite. The chloroform layer was separated, washed with 200 ml of aqueous 30% potassium iodide and with 250 ml of water, dried, and concentrated. The residual foamed glass was freed of additional 6-benzamidopurine by redissolving in chloroform, chilling the solution, filtering through Celite, and concentrating to give 10 g of residue. Medium intensity bands in the ir spectrum at 6.20 and 6.30 μ, as expected for a purine-9-nucleoside, were clearly seen; a band at 6.09 μ indicated the presence of a little 7-nucleoside. Three nucleoside components were observed by tlc in $CHCl_3$–MeOH (95:5), β-9-**30** at R_f 0.80, α-9-**30** at R_f 0.75, both α- and β-**7-30** at R_f 0.45, in addition to sugar impurities at the solvent front and 6-benzamidopurine near the origin.

A solution of the residue in 25 ml of chloroform was added to a chromatographic column (Chromatronix, 100 × 5.0 cm) containing 750 g of silica gel H (10–40 mesh) in chloroform. It was eluted at 500 ml/hr (under 40–50 psi pressure) with chloroform, and the following fractions were collected and analyzed by tlc.

(1) 8.5 l., contained sugars, but no nucleoside, discarded.

(2) 3.6 l., afforded 4.1 g (34%) of crude β-9-**30**, containing a little α-9-**30** and minor sugar impurities; ir 5.79 (strong), 6.20 and 6.31 μ (medium); nmr τ 1.30 s and 1.81 s (2-H, 8-H), 3.75 d (1′-H), 4.08 q (3′-H), 5.25 q (2′-H), 8.02 s (SCH_3), $J_{1',2'}$ = 9.0, $J_{2',3'}$ = 6.0, $J_{3',4'}$ = 2.0 Hz.

Anal.[28] Calcd for $C_{32}H_{27}N_5O_6S$: C, 63.0; H, 4.46; N, 11.5; S, 5.26. Found: C, 62.4; H, 4.37; N, 11.2; S, 4.77.

(3) 6.0 l., afforded 1.2 g (10%) of crude α-9-**30**, containing a little β-9-**30**; ir 5.80 (strong), 6.22 and 6.31 μ (medium); nmr τ 1.26 s and 1.61 s (2-H, 8-H), 3.01 d (1′-H), 4.15 q (3′-H), 5.05 q (4′-H), 5.85 t (2′-H), $J_{1',2'}$ = 7.0, $J_{2',3'}$ = 6.4, $J_{3',4'}$ = 1.8, $J_{4',5'}$ = 4.3 Hz.

(4) 2.8 l., afforded 1.4 g (12%) of crude **7-30**; ir spectra had characteristic bands of a 7 isomer at 6.09 (strong), 6.42 (medium), and 7.63 μ (strong). Presence of both anomers of **7-30** was indicated in the nmr by two distinct quartets for H-2′, at τ 6.12 ($J_{1',2'}$ = 8.8, $J_{2',3'}$ = 5.6 Hz) and 6.25 ($J_{1',2'}$ = 7.3 and $J_{2',3'}$ = 5.5 Hz), by two singlets for SCH_3, narrowly spaced at τ 8.00 and 7.99, and by two singlets for one purine proton (H-2 or H-8, unassigned) at τ 1.41 and 1.20 (the other purine proton was obscured by the benzoyl protons, perhaps as two singlets at τ 1.90 and 1.80). A little α- and β-**9-30** was also detected. Crystallization from methanol afforded 0.7 g (6%) of **7-30**, as the major one of these two anomers: mp 200–205°; ir 5.78 (strong, OBz), 6.08 (strong), 6.24 (medium), 6.6 μ (strong); nmr τ 1.20 s (2-H or 8-H; the other purine H was obscured, perhaps at 1.80, by benzoyl protons; 1′-H was also obscured, below τ 3.0), 4.18 q (3′-H), 6.25 q (2′-H), 8.00 s (SCH_3), $J_{1',2'}$ = 7.3, $J_{2',3'}$ = 5.5, $J_{3',4'}$ = 2.5 Hz.

Anal. Calcd for $C_{32}H_{27}N_5O_6S$: C, 63.0; H, 4.46; N, 11.6; S, 5.26. Found: C, 63.1; H, 4.45; N, 11.6; S, 5.28.

2′-*S*-Methyl-2′-thioadenosine (β-9-33).—A solution of 3.0 g (5.0 mmol) of crude β-9-**30** and 1.4 g of sodium methoxide (27 mmol) in 250 ml of methanol was refluxed for 2 hr, neutralized with 1.6 g of acetic acid, treated with methanolic 10% picric acid until precipitation was complete, chilled, and filtered. The nucleoside picrate that was collected was suspended in 50 ml of water and stirred for 2.5 hr with Dowex 2 (CO_3) resin (30 ml).

The mixture was filtered, and the filtrate was evaporated to give 0.80 g of β-9-33. Recrystallization from acetone gave 0.71 g solvated with acetone, mp 88–92°. Water recrystallization yielded in two crops 0.50 g (33%) without hydration after drying at 100° (1 mm): mp 172–174°; $[\alpha]^{20}D$ −12° (c 0.5, H_2O); ir 5.94 (NH_2), 6.23 μ (aryl); nmr (D_2O) τ 1.78 s and 1.96 s (2-H, 8-H), 4.01 d (1'-H), 5.50 q (3'-H), 5.78 m (4'-H), 6.18 q + d, superimposed (2'-H and 5'-H_2, respectively), 8.21 s (SCH_3), $J_{1',2'}$ = 9.0, $J_{2',3'}$ = 5.6, $J_{3',4'}$ = 2.0 Hz.

Anal. Calcd for $C_{11}H_{15}N_5O_3S$: C, 44.4; H, 5.09; N, 23.6; S, 10.8. Found: C, 44.2; H, 5.22; N, 23.5; S, 10.6.

9-(2-S-Methyl-2-thio-α-D-ribofuranosyl)-9*H*-adenine (α-9-33).—Crude α-9-30 (from fraction 3 above) was deacylated, and the product was isolated through the picrate, as for β-9-33. Purification by preparative tlc in $CHCl_3$–MeOH (4:1) afforded a gum, which could not be crystallized: ir 6.08, 6.25 μ (broad, strong); nmr (D_2O) τ 1.73 s and 1.92 s (2-H, 8-H), 3.49 d (1'-H), 5.54 q superimposed on multiplet at 5.5 (3'-H and 4'-H, respectively), 6.08 q (2'-H), 6.33 uneven d (5'-H_2), 8.10 s (SCH_3), $J_{1',2'}$ = 7.0, $J_{2',3'}$ = 6.0, $J_{3',4'}$ = 1.5, $J_{4',5'}$ = 4.0 Hz.

7-(2-S-Methyl-2-thio-D-ribofuranosyl)-7*H*-adenine (7-33).—Debenzoylation of 1.0 g (1.6 mmol) of crystalline 7-30 (the single anomer, unidentified) with 0.70 g of sodium methoxide was followed by isolation of the product through the picrate, as described for β-9-33. Concentration of the aqueous filtrate to near dryness afforded by crystallization 26 mg (5.5%): mp 195–203°; nmr τ 1.45 s and 1.79 s (2-H, 8-H), 4.04 d (1'-H), 5.60 q (3'-H), 6.06 q (4'-H), 6.30 m (5'-H_2), 6.80 q (2'-H), 8.51 s (SCH_3), $J_{1',2'}$ = 9.5, $J_{2',3'}$ = 7.0, $J_{3',4'}$ = 3.4 Hz.

Anal. Calcd for $C_{11}H_{15}N_5O_3S \cdot H_2O$: C, 41.9; H, 5.43; N, 22.2. Found: C, 41.7; H, 5.46; N, 22.2.

F. Desulfurizations. Methyl 3,4-*O*-Cyclohexylidene-2-deoxy-β-D-ribopyranoside (2). I. From 6.—To 0.90 g (2.6 mmol) of 2-benzylthio 6 dissolved in 125 ml of dry dimethylformamide was added 10 g of sponge nickel.[29] The mixture was protected from moisture and stirred under a GE, 250-W, white heat lamp (distance of 6 in.) for 16 hr and then filtered through Celite. The filter cake was washed with 50 ml of hot dimethylformamide and with 100 ml of hot chloroform, and the combined filtrates were taken to dryness [caution: a sample of 2 was 20% volatilized after 18 hr at 25° (0.75 mm)]. The residue was dissolved in 30 ml of ether, and the solution was washed with 50 ml of sodium bicarbonate and with 50 ml of water, dried, and concentrated. The residue, 0.46 g, by nmr analysis retained 10–15% of unreacted 6, which was removed by preparative tlc on four plates (2-mm thick). The plates were developed with benzene–ether (95:5) and the bands detected with iodine vapor; the brown iodine evaporated without harm to the compound. Chloroform elution of main band afforded 0.34 g (58%) of oil: nmr (100 MHz) τ 5.29 q (1-H), 5.65 doublet of triplets (3-H), 5.93 doublet of triplets (4-H), 6.24 q (5-H_2), 7.91 m and 8.28 m (2-H_2), 8.2–8.8 (cyclohexyl), $J_{1,2a}$ = 6, $J_{1,2e}$ = 4.5, $J_{2a,2e}$ = 15, $J_{2a,3}$ = 4.5, $J_{2e,3}$ = 5.0, $J_{3,4}$ = 6.5, $J_{4,5a}$ and $J_{4,5e}$ = 2.8 and 3.0, $J_{5a,5e}$ estimated 3 Hz. A 100-mg portion was crystallized from methanol–water without changing the nmr spectrum to give 38 mg (6.5%), mp 51–53°, $[\alpha]^{22}D$ −97° ($CHCl_3$). Mixture melting point with the sample from II was 51–53°.

II. From 2-Deoxyribose.—Methyl 2-deoxy-β-D-ribopyranoside (1): mp 30–45° (lit.[8] 83–84° for the L isomer); nmr τ 5.21 t (1-H, $J_{1,2a}$ = $J_{1,2e}$ = 3 Hz), 6.63 s (OCH_3), contained *ca.* 15% of the α anomer, 4.92 q (1-H), 6.56 s (OCH_3). It was converted to the cyclohexanone ketal as described for 4. The product was partitioned between ether and water, and the ether residue was crystallized from methanol–water, mp 52–53°.

Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.1; H, 8.83. Found: C, 63.1; H, 8.84.

(29) Davison Chemical Division, W. R. Grace, and Co.; prewashed with dimethylformamide, wet weight.

9-(2-Deoxy-α-D-ribofuranosyl)adenine from α-9-28.—The sample of α-9-28 (65 mg, 0.10 mmol, mainly α) was desulfurized in 50 ml of dimethylformamide with 1 g of sponge nickel[29] under a heat lamp as described for 2. The hot solution was filtered, the filter cake was washed with 100 ml of chloroform, and the combined filtrate was concentrated. The residual brown oil (190 mg) showed little or no nmr signal for C_6H_5 of benzyl. It was subjected to mild deacylation in 10 ml of methanol with 1 ml of diisopropylamine at reflux for 3 hr. After evaporation the residue was partitioned between 10 ml of water and 10 ml of chloroform. The water layer was evaporated to give 15 mg (57%) of crude α anomer of deoxyadenosine, identified by direct, simultaneous comparison with authentic samples of deoxyadenosine and its anomer[30] on tlc. Three developments of the plate with $CHCl_3$–MeOH (4:1) gave good resolution, R_f 0.50 for the α anomer, R_f 0.60 for deoxyadenosine. The desulfurization product had a strong spot at R_f 0.50, a faint spot at R_f 0.60, and traces of faster moving contaminants.

2'-Deoxyadenosine. I. From 2'-S-Benzyl-2'-thioadenosine (β-9-31).—A sample (92 mg, 0.25 mmol) of β-9-31 was desulfurized with 1 g of sponge nickel in 50 ml of dimethylformamide. The hot mixture was filtered, and the filter cake was washed with 50 ml of hot dimethylformamide, 50 ml of methanol, and 100 ml of water. Concentration of the combined filtrates afforded 20 mg. The nmr showed it was a mixture (2:1) of 2'-deoxyadenosine and unreacted β-9-31; direct comparison on tlc, as above, confirmed the presence of 2'-deoxyadenosine and showed the absence of any α anomer. Pure 2'-deoxyadenosine (5 mg, 8%) was separated by preparative tlc on one plate (1-mm thick) developed twice with chloroform–methanol (4:1).

II. From β-9-30.—Similarly, desulfurization of β-9-30 followed by debenzoylation of the intermediate with methanolic sodium methoxide afforded 2'-deoxyadenosine free of the α anomer, by direct comparison on tlc, as decsribed for α-9-28.

Registry No.—2, 30545-66-5; 4, 30545-67-6; 5, 30545-68-7; α-6, 30545-69-8; β-6, 30545-70-1; 7, 30545-71-2; 8, 30545-78-9; 10, 30538-24-0; 13, 30538-25-1; 14, 30538-26-2; 15, 30538-27-3; 16, 30538-28-4; α-17, 30538-29-5; β-17, 30538-30-8; α-18, 30651-47-9; β-18, 30538-31-9; α-19, 30538-32-0; β-19, 30538-33-1; α-23, 30538-34-2; β-23, 30538-35-3; α-24, 30538-36-4; β-24, 30538-37-5; α-25, 30538-38-6; β-25, 305-38-39-7; α-26, 30597-74-1; β-27, 30538-40-0; α-9-27, 30545-79-0; β-9-27, 30545-80-3; 7-28, 30545-72-3; α-9-28, 30545-81-4; β-9-28, 30545-82-5; 7-29, 30545-73-4; β-9-29, 30545-83-6; α-7-30, 30546-00-0; β-7-30, 30545-74-5; α-9-30, 30545-84-7; β-9-30, 30545-85-8; 7-31, 30545-75-6; α-9-31, 30597-72-9; β-9-31, 30545-86-9; 7-32, 30545-76-7; α-9-32, 30545-87-0; β-9-32, 30545-88-1; 7-33, 30545-77-8; α-9-33, 30597-73-0; β-9-33, 30545-89-2; 34a, 30545-90-5; 34b, 30545-91-6; 35, 30538-41-1; 36, 6984-53-8; 37, 23819-18-3; 38, 30538-43-3; 39, 485-08-5.

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