Introduction of a 2′,3′ Double Bond into Purine Ribonucleosides by Selective Elimination Reactions

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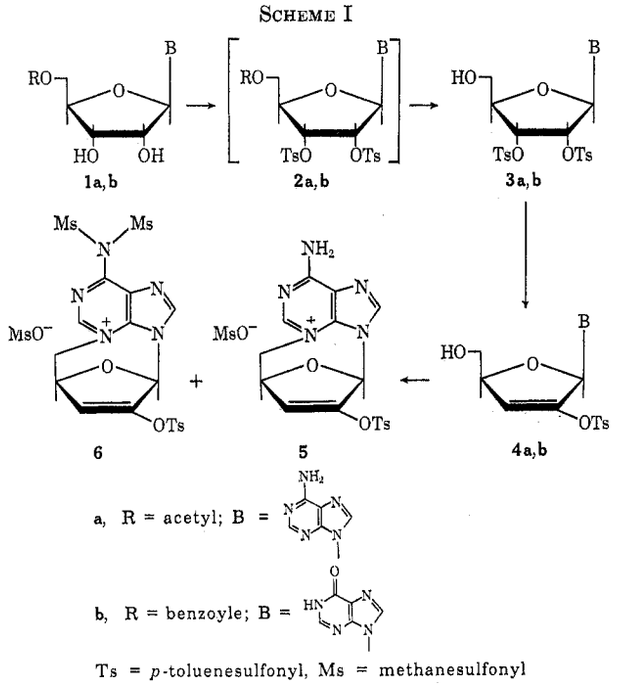
To investigate the direction of base-induced elimination reactions on 2′,3′-di-*O*-tosyl derivatives of purine ribonucleosides, 2,′3′-di-*O*-tosyladenosine (**3a**) and 2′,3′-di-*O*-tosylinosine (**3b**) were synthesized from 5′-acetyladenosine (**1a**) and 5′-benzoylinosine (**1b**) through ditosylation and 5′ deprotection. Sodium methoxide catalyzed elimination reactions on **3a–b** only gave the corresponding 2′,3′-didehydro purine nucleosides (**4a–b**) with a tosyl group at C_2'. Mesylation of **4a** gave 3′-deoxy-2′-*O*-tosyl-2,′3′-didehydro-3,5′-cycloadenosine mesylate (**5**) and its N^6-dimesylated derivative (**6**).

In previous papers,[1,2] the results of some base-catalyzed elimination reactions with the 2′,3′-di-*O*-mesyl derivatives of 3-benzyluridine and 1-(5′-*O*-benzoyl-β-D-lyxofuranosyl)uracil, as well as with the 2′-*O*-tosyl- (or -mesyl-) 3′-*O*-mesyl (or -tosyl) derivative of the latter compound have been described. In these reactions, 2′ hydrogen was always vulnerable to attack by basic catalysts, giving rise to 2′-uridinenes with a leaving group at C_2'.

The study has now been extended to similar elimination reactions with derivatives of some purine ribonucleosides in order to establish the generality of the selective 2′-hydrogen abstraction in the trans-elimination reactions of 2′,3′-di-*O*-mesyl (or -tosyl) derivatives of ribonucleosides. In this study, the 2′,3′-di-*O*-tosyl derivatives of adenosine and inosine were chosen as substrates for elimination reactions as shown in Scheme I.

SCHEME I



Ts = *p*-toluenesulfonyl, Ms = methanesulfonyl

5′-*O*-Acetyladenosine[3] was treated with excess tosyl chloride to give 5′-*O*-acetyl-2′,3′-di-*O*-tosyladenosine (**2a**), which was directly converted to 2′,3′-di-*O*-tosyladenosine (**3a**). The ditosylation procedure presented some troubles, presumably for steric reasons, and always resulted in mixtures containing minor products as indicated by tlc, one of which seemed to be 2′-*O*-monotosylated derivative.[4] Deacetylation of **2a** with ammonia in methanol was also accompanied by some side reactions. In the present case, these side products were neglected and the synthetic procedure for **3a** was standardized as described in the Experimental Section.

5′-*O*-Benzoylinosine (**1b**) was obtained from 5′-*O*-benzoyl-2′,3′-*O*-isopropylideneinosine[5] by hydrolysis with 10% acetic acid. The formation of **1b** in a rather too low yield (60%) was due to depurination, which was confirmed by the separation and characterization of some hypoxanthine in a separate experiment. Compound **1b** was similarly converted to 2′,3′-di-*O*-tosylinosine (**3b**). Compounds **3a–b** were now allowed to react with sodium methoxide at 100° to give 9-(3′-deoxy-2′-*O*-tosyl-β-D-*glycero*-pent-2′-enofuranosyl)-adenine (**4a**) and 9-(3′-deoxy-2′-*O*-tosyl-β-D-*glycero*-pent-2′-enofuranosyl)hypoxanthine (**4b**) in 55 and 37% yield, respectively, regenerating some starting material. Under the particular reaction conditions described in the Experimental Section, no other products were detected by tlc.[6] It must be noted that the reaction did not occur at ambient temperature, in contrast with the reported similar elimination reaction of 3′-*O*-tosyl-2′-deoxyadenosine.[7]

Structure assignments of **4a** and **4b** are essentially based on their nmr spectra, which exhibited similar resonance patterns for $H_{1'}$, $H_{3'}$, and $H_{4'}$. The appearance of a doublet of doublets for $H_{3'}$, a triplet for $H_{1'}$, and an octet for $H_{4'}$ in this order upfield are characteristic of this type of furanose-ene protons.[1,2] Reasons for the assignments of these signals were detailed previously.[1] Although in the case of **4b** the signal of $H_{4'}$ is not well resolved (see Experimental Section), the structure assigned is justified by the presence of a triplet for $H_{1'}$ and a doublet of doublets for $H_{3'}$ at 6.10 and 6.62 ppm, respectively.[8] Thus, selectivity in the

(1) T. Sasaki, K. Minamoto, and H. Suzuki, *J. Org. Chem.*, **38**, 598 (1973).

(2) T. Sasaki, K. Minamoto, and K. Hattori, *J. Org. Chem.*, in press.

(3) D. M. Brown, L. J. Haynes, and A. R. Todd, *J. Chem. Soc.*, 3299 (1950).

(4) A. Todd and T. L. V. Ulbricht, *J. Chem. Soc.*, 3276 (1960).

(5) M. Ikehara, H. Uno, and F. Ishikawa, *Chem. Pharm. Bull.*, **12**, 267 (1964).

(6) The results described here are the best of several experiments. Heating the reaction mixtures until the complete disappearance of the starting materials caused a couple of side-products to form. Reactions of **3a–b** with sodium benzoate in DMF were also examined, when trivial amounts of **4a–b** were obtained with intractable by-products.

(7) J. R. McCarthy, Jr., M. J. Robins, L. B. Townsent, and R. K. Robins, *J. Amer. Chem. Soc.*, **88**, 1549 (1966).

(8) If an alternative structure, in which the tosyl group is linked to $C_{3'}$, were concerned, the signals of $H_{1'}$ and $H_{2'}$ should appear as the same doublet of doublets with a relative intensity of 1:1:1:1, and equal splittings of 1.7 Hz.[1]

trans-elimination reactions was also proved in the series of purine ribonucleosides.

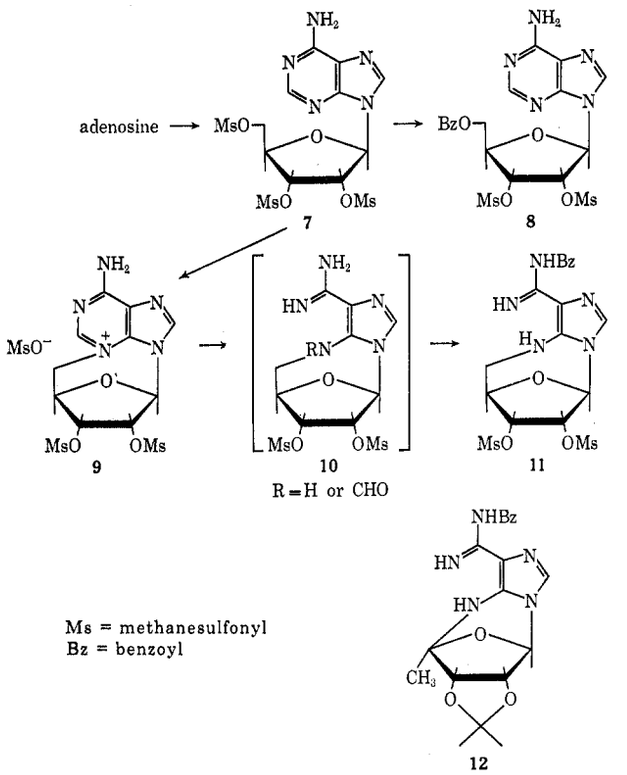
This effect could be due to the electron-deficient nature of $C_{2'}$ (and hence the high acidity of $H_{2'}$) stemming from the electron-withdrawing force of the base moiety in nucleosides. The generally observed, selective or quasiselective alkylation or acylation of 2′-OH might also be interpreted in the same sense.[9] The particularly high selectivity in the elimination reactions, irrespective of possible steric influences by the size of the basic portion or substituent at $C_{5'}$,[1,2] would be connected with the fact that 2′ hydrogen concerned can be directly influenced by the electron-deficient $C_{2'}$, while in alkylation or acylation of 2′-OH the effect of $C_{2'}$ might be reduced to some extent by the participation of the electron-rich oxygen atom.

Treatment of **4a** with mesyl chloride easily gave 3′-deoxy-2′-*O*-tosyl-2′,3′-didehydro-3,5′-cycloadenosine mesylate (**5**), the first 3,5′-cyclopurine ribonucleoside with a double bond in the sugar moiety. The quaternized structure (**5**) was clear on the basis of its ultraviolet absorption at 274 nm in contrast with that of **4a** at 258 nm. On treatment of **4a** with excess mesyl chloride at ambient temperature, N^6-dimesyl-3′-deoxy-2′-*O*-tosyl-2′,3′-didehydro-3,5′-cycloadenosine mesylate (**6**) was obtained with a small amount of **5**. The structure of **6** is based on its analysis and ultraviolet (219 and 269 nm) and nuclear magnetic resonance spectrum.[10] Interestingly, the nmr spectrum of **6** retained the characteristic furanose-ene proton resonances, *i.e.*, a triplet for $H_{1'}$ at 6.34 ppm and a doublet of doublets for $H_{3'}$ at 6.82 ppm with the same coupling constants as in the case of **4a**. This seems to explain the extremely facile cyclization at N^3, by which no substantial steric strain is generated to cause a conformational modification in the unsaturated sugar skeleton.

Although didehydro nucleosides **4a–b** were formed selectively from **3a–b**, their use as versatile synthetic intermediates seemed questionable, since the synthetic routes leading to the didehydro nucleosides **4a** and **4b** involved six steps starting from adenosine or inosine and their overall yields based upon **1a–b** were only 20–30%. Repeated attempts to separate **4a–b** or their analogs from the reaction mixtures obtained by the action of sodium benzoate or sodium methoxide on crude or semipurified **2a** and **2b** were unsuccessful.

At this stage, a path *via* 2′,3′,5′-tri-*O*-mesyl purine nucleosides was considered to be more economical, since Mizuno, *et al.*,[11] had succeeded in phosphorylating the 5′ position of N^6-acetyl-3,5-cycloadenosine and hence 5′-*O*-benzoyl-2′,3′-di-*O*-mesyl purine nucleosides seemed to be more easily accessible *via* an analogous route. Hence, a series of preliminary synthetic work (without N^6-acetylation) was carried out as shown in Scheme II. 2′,3′,5-Tri-*O*-mesyladenosine (**7**) obtained

SCHEME II



by the standard method was allowed to react with sodium benzoate in DMF at a rather high temperature, with the expectation that elimination might take place concomitantly. However, this reaction yielded only a limited amount of a water-insoluble product mixture, from which 5′-*O*-benzoyl-2′,3′-di-*O*-mesyladenosine (**8**) was isolated as the major product in 13.5% yield.

The location of the introduced benzoyl group as in structure **8** was evident from the nmr spectrum, in which the resonances of the tosyl-deshielded protons, $H_{2'}$ and $H_{3'}$, appeared at δ 6.22 ($J_{1',2'} = J_{2',3'} = 5.0$ Hz) and 5.97 ($J_{2',3'} = 5.0$, $J_{3',4'} = 4.2$ Hz), respectively, and are distinctly separated from the resonance envelope of $H_{4'}$ and $H_{5'}$ at δ 4.43–4.82 (see Experimental Section). It was thus concluded that most of the starting material **7** was lost in the form of water-soluble products after quaternization at N^3.

To clear up this point, **7** was converted to 2′,3′-di-*O*-mesyl-3,5′-cycloadenosine mesylate (**9**), which was treated with equimolar sodium benzoate under mild conditions to remove only the mesylate anion. The obtained water-soluble product (**10**, R = H or CHO)[12] was benzoylated to give N^5,5′-anhydro(5′-deoxy-2′,3′-di-*O*-mesyl-β-D-ribofuranosyl)-4-(*N*-benzoylcarboxamidino)-5′-aminoimidazole (**11**) as pale yellow crystals. Its structure was easily deduced from its characteristic

(9) See, for example, (a) N. C. Young and J. J. Fox, *J. Amer. Chem. Soc.*, **83**, 3060 (1961) (synthesis of 2′,5,-di-*O*-trityluridine). Although concomitant formations of 3′-O-substituted isomers of nucleoside derivatives have been known,[9b–e] their yields are usually lower than those of 2′ isomers. (b) J. Zemlicka, *Collect. Czech. Chem. Commun.*, **29**, 1734 (1964) (tritylation). (c) A. F. Cook and J. G. Moffatt, *J. Amer. Chem. Soc.*, **89**, 2697 (1967) (tritylation). (d) L. F. Christensen and A. D. Broom, *J. Org. Chem.*, **37**, 3398 (1972) (benzylation). (e) M. Ikehara and H. Tada, "Synthetic Procedures in Nucleic Acid Chemistry," Vol. 1, W. W. Zorbach and R. S. Tipson, Ed., Interscience, New York, N. Y., 1968, p 188 (tosylation).

(10) Another structure with a mesyl group on N^1 and a second on N^6 might also be considered. At the present stage, however, we like to propose structure **6** based on its nmr spectrum, in which the signals of two mesyl groups appeared at 3.84 ppm as a sharp six-proton singlet. While no appropriate literature analog is available for direct uv spectral comparison, the absorption at 269 nm does not conflict with structure **6**, considering that a 5-nm hypsochromic shift was caused by blocking the amino group in **5** with the mesyl groups.

(11) Y. Mizuno and T. Sasaki, *J. Amer. Chem. Soc.*, **88**, 863 (1966).

(12) It is not clear when the formyl group was lost. We only suggest the possibility of its hydrolytic cleavage during the work-up of the reaction mixture from **9** and sodium benzoate, since the reaction mixture should have contained benzoic acid released from sodium benzoate, and further the experiment was not carried out under absolutely anhydrous conditions. A similar facile cleavage of a corresponding *N*-formyl group has been described.[13]

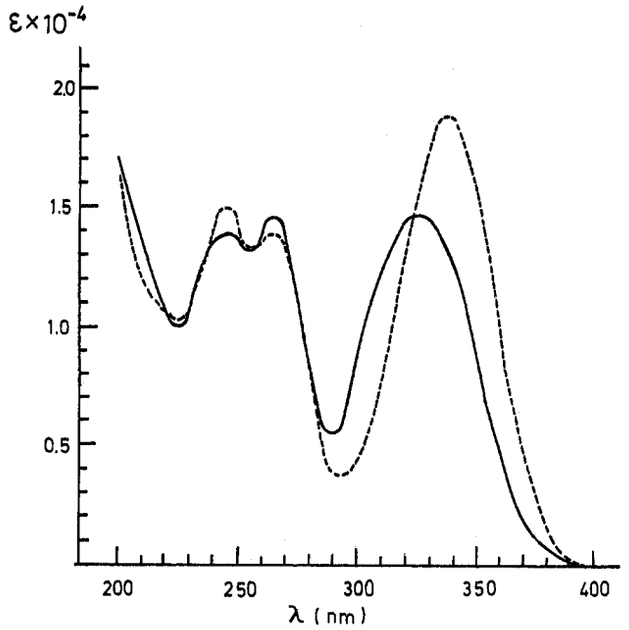


Figure 1.—Ultraviolet spectra of N^6,5′-anhydro-(5′-deoxy-2′,3′-di-*O*-mesyl-β-D-ribofuranosyl)-4-(*N*-benzoylcarboxamidino)-5′-aminoimidazole (**11**) (——) and N^6,4-anhydro(5′-deoxy-2′,3′-*O*-isopropylidene-α-L-lyxosyl)-4-benzoylcarboxamidino-5-aminoimidazole (**12**) (- - - -) in ethanol.

uv absorption comparable with that of N^6,4-anhydro-(5′-deoxy-2′,3′-*O*-isopropylidene-α-L-lyxosyl)-4-benzoylcarboxamidino-5-aminoimidazole (**12**)[13] (Figure 1). The bathochromic shift (10 nm) of the longest wavelength absorption of **12** as compared with that of **11** seems to reflect the extension of the π conjugation of the base up to the ether oxygen of the furanose ring. A similar decomposition of a N^3-quaternized N^6-dimethyladenosine analog by barium hydroxide solution has previously been reported.[14] Thus, this series of experiments with **7** failed to give a didehydro nucleoside. It appears, however, that the tri-*O*-mesylate route, needs to be more thoroughly investigated.

Experimental Section

All the melting points are uncorrected. The electronic spectra were measured on a Jasco Model ORD/UV-5 spectrophotometer. The nmr spectra were recorded with a JNM C-60 HL spectrometer, TMS being used as an internal standard. In the case of the hydroxyl and/or NH-containing compounds, measurements after D_2O exchanges were also carried out. Wakogel B-5 silica gel, supplied by the Wako Pure Chemical Industries, Ltd., was used for thin layer chromatography. Elemental microanalyses were performed with a Perkin-Elmer 240 elemental analyzer in this laboratory.

5′-*O*-Benzoylinosine (1b).—5′-*O*-Benzoyl-2′,3′-*O*-isopropylideneinosine (1.5 g, 3.64 mmol) was heated in 10% acetic acid (100 ml) at 90° for 4 hr. The mixture was evaporated to a semisolid residue, which was dissolved in ethanol and again evaporated. This procedure was repeated to remove the residual acetic acid. The solid was dissolved in hot water and a small amount of insoluble material was removed by filtration. Concentration of the filtrate gave crystals, which were repeatedly crystallized from water to give colorless needles (0.85 g, 60%): mp 147–149°; λ_{max}^{EtOH} 230 nm (ε 18,400), 248 (12,100, inflection), and 260 (6700, inflection).

Anal. Calcd for $C_{17}H_{16}N_4O_6 \cdot H_2O$: C, 52.30; H, 4.65; N, 14.35. Found: C, 52.42; H, 4.78; N, 14.46.

2′,3′-Di-*O*-tosyladenosine (3a).—5′-*O*-Acetyladenosine (**1a**) (1.39 g, 4.5 mmol) was dissolved in anhydrous pyridine (6 ml) and treated with tosyl chloride (2.22 g, 11.6 mmol) at 0° overnight. The reaction mixture was added with ethanol (2 ml), left at room temperature for 30 min, and poured into ice–water (100 ml) under vigorous stirring. The collected precipitate was dissolved in chloroform and the chloroform solution was washed with 5% sodium bicarbonate and water in this order and dried with sodium sulfate. Evaporation of the solvent gave 2.54 g of a foam, which was dissolved in a mixture of methanol (75 ml) and concentrated ammonia (25 ml). After stirring at room temperature for 5 hr, the mixture was evaporated at below 40° to a semisolid residue, which was triturated with a small amount of ethanol to give crystals that were filtered and repeatedly crystallized from ethanol to colorless needles (1.36 g, 53%), mp 207–209°, λ_{max}^{EtOH} 226 nm (ε 23,000) and 260 (12,500).

Anal. Calcd for $C_{24}H_{25}N_5O_9S_2$: C, 50.09; H, 4.38; N, 12.17. Found: C, 50.28; H, 4.42; N, 11.88.

2′,3′-Di-*O*-tosylinosine (3b).—5′-*O*-Benzoylinosine (**1b**) (2.89 g, 7.4 mmol) was repeatedly coevaporated with ethanol to remove the water of crystallization and dried under high vacuum for 24 hr. This material was treated with tosyl chloride (3.53 g, 18.5 mmol) in anhydrous pyridine (9 ml) at room temperature overnight. An aliquot of the mixture was examined by tlc to show the presence of some starting material. Therefore, additional tosyl chloride (0.5 g) was added to the reaction mixture and the total was kept at 40–45° for a further 4 hr, added with ethanol (1 ml) after cooling, and poured into stirred ice–water (150 ml). The separating solid was filtered by suction, dissolved in chloroform while wet, and washed with dilute sodium bicarbonate solution and water. The chloroform solution was dried with sodium sulfate and evaporated *in vacuo* to give a foam, which was taken into a mixture of methanol (180 ml) and concentrated ammonia (60 ml) and stirred at room temperature for 5 hr. The reaction mixture was evaporated *in vacuo* at below 40° to a syrup, which was digested with ether, and the ether washing was decanted off. Recrystallization of the residue from methanol gave 2.0 g (65%) of colorless needles: mp 249–252°; λ_{max}^{EtOH} 226 nm (ε 26,100), 250 (9700, inflection), and 268 (6600, inflection); nmr ($CDCl_3$–DMSO-d_6) δ 2.33 (3 H, s, methyl), 2.48 (3 H, s, methyl), 3.64 (2 H, d, $H_{5'}$), 4.10 (1 H, br s, OH, D_2O exchangeable), 4.34 (1 H, br s, $H_{4'}$), 5.17 (1 H, d, $J_{2',3'}$ = 5.4 Hz, $H_{3'}$), 5.40 (1 H, dd, $J_{1',2'}$ = 7.4, $J_{2',3'}$ = 5.4 Hz, $H_{2'}$), 6.10 (1 H, d, $J_{1',2'}$ = 7.4 Hz, $H_{1'}$), 6.95–7.95 (8 H, m, aromatic protons of the tosyl groups), 7.71 (1, H, s, H_2 or H_8), 8.04 (1 H, s, H_8 or H_2), and 12.31 (1 H, br s, NH, D_2O exchangeable).

Anal. Calcd for $C_{24}H_{24}N_4O_9S_2$: C, 49.99; H, 4.20; N, 9.72. Found: C, 49.75; H, 4.30; N, 9.94.

9-(3′-Deoxy-2′-*O*-tosyl-β-D-*glycero*-pent-2′-enofuranosyl)adenine (4a).—2′,3′-Di-*O*-tosyladenosine (**3a**) (1.1 g, 1.91 mmol) and sodium methoxide (0.49 g, 9.6 mmol) were combined in *N*,*N*-dimethylformamide (DMF) (15 ml) and the mixture was heated at 100° for 80 min under stirring. The mixture was evaporated *in vacuo* at a bath temperature of 55° to a paste, which was dissolved in methanol (10 ml) and neutralized with acetic acid. The methanol was removed by evaporation and the residue was extracted with chloroform (4 × 50 ml) under the presence of water (20 ml). The chloroform solution was dried with sodium sulfate and evaporated to a solid residue, which was repeatedly crystallized from methanol to afford colorless needles (**4a**): mp 209–210°; yield 0.42 g (55%); λ_{max}^{EtOH} 228 nm (ε 14,500) and 258 (14,300); nmr (DMSO-d_6) δ 2.41 (3 H, s, methyl of the tosyl), 5.25 (1 H, br s, OH, D_2O exchangeable), 3.61 (2 H, br s, $H_{5'}$), 4.90 (1 H, octet, $J_{1',4'}$ = 1.6, $J_{3',4'}$ = 3.1, $J_{4',5'}$ = 3.1 Hz, $H_{4'}$), 6.17 (1 H, t, $J_{1',4'}$ = 1.6, $J_{1',3'}$ = 1.6 Hz, $H_{1'}$), 6.63 (1 H, dd, $J_{1',3'}$ = 1.6, $J_{3',4'}$ = 3.1 Hz, $H_{3'}$), 7.25 (2 H, br s, NH_2, lost on D_2O addition), 7.33 (2 H, d, *J* = 8.3 Hz, tosyl protons ortho to the methyl group), 7.66 (2 H, d, *J* = 8.3 Hz, tosyl protons meta to the methyl), 8.02 (1 H, s, H_2 or H_8), and 8.04 (1 H, s, H_8 or H_2).

Anal. Calcd for $C_{17}H_{17}N_5O_5S$: C, 50.62; H, 4.25; N, 17.36. Found: C, 50.44; H, 4.30; N, 17.13.

9-(3′-Deoxy-2′-*O*-tosyl-β-D-*glycero*-pent-2′-enofuranosyl)hypoxanthine (4b).—A mixture of 2′,3′-di-*O*-tosylinosine (**3b**) (1.125 g, 1.94 mmol) and sodium methoxide (0.65 g, 11.8 mmol) in DMF (12 ml) was heated at 100° for 1 hr. After almost all the solvent was evaporated *in vacuo*, the residue was dissolved in methanol (10 ml) and neutralized with acetic acid and the mix-

(13) T. Sasaki, K. Minamoto, and K. Hattori, *J. Amer. Chem. Soc.*, **95**, 1350 (1973).

(14) B. R. Baker and J. P. Joseph, *J. Amer. Chem. Soc.*, **77**, 15 (1955).

ture was again evaporated *in vacuo* at below 40°. The brown-colored residue was taken up in chloroform (150 ml), and the solution was washed with a small amount of water and dried over sodium sulfate. Evaporation of the solvent gave a paste, which gave 0.15 g of a colorless wool (**4b**) from acetone. The filtrate was concentrated and submitted to preparative thin layer chromatography with the use of a silica gel plate and a solvent mixture, ethanol–benzene (2:8 v/v), to give a second crop of crude **4b** (0.16 g). The combined product was recrystallized from acetone to give 0.29 g (37%) of colorless wool (**4b**): mp 148–149°; λ_{max}^{EtOH} 230 nm (ε 14,600), 248 (10,500), inflection), 263 (5600, inflection), and 271 (4400, inflection); nmr ($CDCl_3$ + DMSO-d_6) δ 2.08 (3 H, $\frac{1}{2}CH_3COCH_3$), 2.38 (3 H, methyl of the tosyl), 3.73 (2 H, d, $J_{4',5'}$ = 2.8 Hz, 2 $H_{5'}$), 4.30 (1 H, br s, OH, lost on D_2O addition), 4.95 (1 H, br m, $H_{4'}$), 6.10 (1 H, t, $J_{1',3'}$ = 1.7, $J_{1',4'}$ = 1.7 Hz, $H_{1'}$), 6.62 (1 H, dd, $J_{3',4'}$ = 3.2, $J_{1',3'}$ = 1.7 Hz, $H_{3'}$), 7.27 (2 H, d, J = 8.6 Hz, tosyl protons ortho to the methyl), 7.62 (2 H, d, J = 8.6 Hz, tosyl protons meta to the methyl), 7.85 (1 H, s, H_2 or H_8), 7.99 (1 H, s, H_8 or H_2), and 12.28 (1 H, br s, NH, D_2O exchangeable).

Anal. Calcd for $C_{17}H_{16}N_4O_6S \cdot \frac{1}{2}CH_3COCH_3$: C, 51.27; H, 4.42; N, 12.93. Found: C, 51.48; H, 4.49; N, 12.88.

The analysis values did not significantly change on drying the sample at 60–65° under high vacuum for 24 hr.

From the faster moving band of the tlc plate, *ca.* 0.1 g of the starting material was recovered.

3′-Deoxy-2′-*O*-tosyl-2′,3′-didehydro-3,5′-cycloadenosine Mesylate (5).—9-(3′-Deoxy-2′-*O*-tosyl-β-D-*glycero*-pent-2′-enofuranosyl)adenine (**4a**) (0.1 g, 0.25 mmol) was dissolved in anhydrous pyridine (1.5 ml) and added with mesyl chloride (0.02 ml, 0.26 mmol) at 0° with stirring. After standing at 0° overnight, the mixture was poured into ice–water (15 ml) to give a pasty precipitate, which was separated from the water, dissolved in chloroform, and dried over sodium sulfate. Evaporation of the solvent gave a brown paste, an aliquot of which was examined by tlc with the use of a silica gel plate and a mixed solvent, ethanol–benzene (2:8), to show the complete conversion of **4a** to a mixture (approximately in 2:1 ratio) of a faster moving substance (5′-*O*-mesylated derivative of **4a**) and an immobile substance (**5**). The total mixture was refluxed in acetone to give a crystalline precipitate (**5**), which was filtered. The filtrate was concentrated and again heated in acetone to give another crop of **5**. The total product was recrystallized from a mixture of acetone and methanol to give 80 mg (67%) of colorless prisms of **5**: mp 175–177°; λ_{max}^{EtOH} 216 nm (ε 18,800) and 274 (12,600).

Anal. Calcd for $C_{18}H_{19}N_5O_7S_2 \cdot \frac{1}{2}H_2O$: C, 44.08; H, 4.11; N, 14.28. Found: C, 44.23; H, 4.05; N, 14.14.

N^6-Dimesyl-3′-deoxy-2′-*O*-tosyl-2′,3′-didehydro-3,5′-cycloadenosine Mesylate (6).—**4a** (0.17 g, 0.42 mmol) was dissolved in anhydrous pyridine (1 ml) and added with mesyl chloride (0.05 ml, 0.64 mmol) and the mixture was left at room temperature overnight. The red-colored mixture was poured into ice–water (30 ml) to give a precipitate, which was filtered, dried by pressing on a porous plate, and dissolved in hot acetone. Sparingly soluble crystals (20 mg) were filtered and infrared spectroscopically identified with compound **5** after recrystallization from a mixture of acetone and methanol. The acetone solution separated from **5** was concentrated to a gum, which solidified on scratching with a spatula in the presence of a small amount of methanol. Repeated recrystallization of the solid from a mixture of methanol and acetone gave 80 mg of colorless needles (**6**): mp 156° λ_{max}^{EtOH} 219 nm (ε 14,100) and 269 (10,800); nmr (DMSO-d_6) δ 2.38 (3 H, s, methyl in the tosyl group), 3.07 (3 H, s, mesylate anion), 3.84 (6 H, s, two mesyl on N^6), 4.46 (2 H, d, J = 4.0 Hz, 2 $H_{5'}$), 5.23 (1 H, m, $H_{4'}$), 6.34 (1 H, t, $J_{1',3'}$ = $J_{1',4'}$ = 1.6 Hz, $H_{1'}$), 6.82 (1 H, dd, $J_{1',3'}$ = 1.6, $J_{3',4'}$ = 3.1 Hz, $H_{3'}$), 7.28 (2 H, J = 8.4 Hz, tosyl protons), 7.55 (2 H, J = 8.4 Hz, tosyl protons), 8.47 (1 H, s, H_2 or H_8), and 8.78 (1 H, s, H_8 or H_2).

Anal. Calcd for $C_{20}H_{23}N_5O_{11}S_4$: C, 37.68; H, 3.64; N, 10.99. Found: C, 37.64; H, 3.60; N, 10.95.

Tlc on the filtrate of **6** exhibited the presence of two faster moving substances (presumably unquaternized isomers corresponding to compound **5** and **6**), which were discarded.

2′,3′,5′-Tri-*O*-mesyladenosine (7) and 2′,3′-Di-*O*-mesyl-3,5′-cycloadenosine Mesylate (9).—To an ice-cold stirred solution of adenosine (1 g, 3.78 mmol) in anhydrous pyridine (20 ml) was gradually added mesyl chloride (0.94 ml, 12 mmol). After standing at 0° overnight, the mixture was added with ethanol (3 ml), left at room temperature for 20 min, and concentrated to a gum at below 40°. The gum was taken into methanol (10 ml) and precipitated into ice–water (100 ml). The separated precipitate was dissolved in ethyl acetate (50 ml), dried over sodium sulfate, and evaporated *in vacuo* to an essentially pure foam (**7**) (1.2 g, 64%) at below 40°. A portion of the product was further purified by tlc with the use of silica gel and ethanol–benzene (2:8) for elemental analysis.

Anal. Calcd for $C_{13}H_{19}N_3O_{10}S_3$: C, 31.14; H, 3.82; N, 13.97. Found: C, 30.94; H, 3.98; N, 14.08.

7 (0.4 g) was refluxed in acetone (10 ml) for several hours to yield a solid precipitate, which was filtered and washed with acetone (0.2 g). The filtrate was again heated to reflux for 3 hr and left at room temperature for 1 week to give an additional precipitate (0.15 g), which was filtered, combined with the product obtained above, and recrystallized from methanol to afford 0.32 g (80%) of colorless powder: mp 185–195° dec; λ_{max}^{EtOH} 274 nm (ε 12,500).

Anal. Calcd for $C_{13}H_{19}N_5O_{10}S_3$: C, 31.14; H, 3.82; N, 13.97. Found: C, 30.87; H, 4.05; N, 13.78.

Reaction of Sodium Benzoate with 2′,3′,5′-Tri-*O*-mesyladenosine (7). Separation of 5′-*O*-Benzoyl-2′,3′-di-*O*-mesyladenosine (8).—**7** (0.5 g, 1 mmol) and sodium benzoate (0.3 g, 2.1 mmol) were combined in DMF (10 ml) and the mixture was stirred at 120° for 1 hr and then at 130° for 40 min. After cooling, the mixture was evaporated *in vacuo* to a gum, which was digested with ice–water (40 ml). The insoluble part was filtered, dried by pressing on a porous plate, and checked by tlc using silica gel and ethanol–benzene (2:8) to show one main and two minor spots. Preparative thin layer chromatography with the use of the same solvent system gave crystals of mp 158–162° from the major band, which were recrystallized from acetone to give 80 mg (13.5%) of colorless needles: mp 162–164°; λ_{max}^{EtOH} 228 nm (ε 14,400) and 255 (14,200); nmr (DMSO-d_6) δ 2.08 (6 H, s, acetone of crystallization), 3.30 (3 H, s, mesyl), 3.40 (3 H, s, mesyl), 4.43–4.82 (3 H, br m, $H_{4'}$ and 2 $H_{5'}$), 5.97 (1 H, dd, $J_{2',3'}$ = 5.0, $J_{3',4'}$ = 4.2 Hz, $H_{3'}$), 6.22 (1 H, t, $J_{1',2'}$ = 5.0, $J_{2',3'}$ = 5.0 Hz, $H_{2'}$), 6.37 (1 H, d, $J_{1',2'}$ = 5.0 Hz, $H_{1'}$), 7.36 (2 H, br s, NH_2, D_2O exchangeable), 7.46–7.65 (3 H, m, phenyl protons), 7.93 (2 H, q, phenyl protons), 7.99 (1 H, s, H_2), and 8.31 (1 H, s, H_8).

N^6,5′-Anhydro(5′-deoxy-2′,3′-di-*O*-mesyl-β-D-ribofuranosyl)-4-(*N*-benzoylcarboxamidino)-5′-aminoimidazole (11).—Compound **9** (0.5 g, 1 mmol) and sodium benzoate (158 mg, 1.1 mmol) were combined in DMF (7 ml) and the mixture was stirred at 95–100° for 20 min. The benzoate salt was smoothly consumed and a clear solution resulted. The mixture was evaporated to a paste, which was repeatedly triturated with ether, and the ether washings were discarded. The residue was extracted with hot acetone (2 × 50 ml) and the acetone solution was filtered with charcoal. Evaporation of the solvent gave a glass (**10**), which was quite soluble in water, acetone, or methanol and resisted crystallization. This basic compound stuck strongly to silicic acid, thus rendering purification by tlc (silica gel) impossible even with the use of a polar solvent system, ethanol–benzene (5:5). Hence, the glass was repeatedly evaporated with dry acetone to a foam and treated with benzoyl chloride (0.14 ml, 1.2 mmol) in pyridine (1.5 ml) under the presence of triethylamine (0.15 ml). After 1 hr of stirring at room temperature, the mixture was evaporated *in vacuo* at below 40° to a paste, which was taken into methanol (5 ml) and dropped into stirred ice–water (50 ml). The precipitate was filtered, dried on a porous plate, and submitted to preparative thin layer chromatography with the use of ethanol–benzene (2:8). Elution of the main band with acetone gave a yellow paste, which was crystallized from a mixture of acetone and methanol to give 0.2 g of pale yellow needles: mp 139–142°; λ_{max}^{EtOH} 244 nm (ε 13,900), 264 (14,500) and 325 (14,800).

Anal. Calcd for $C_{18}H_{21}N_5O_8S_2 \cdot \frac{1}{2}H_2O$: C, 42.92; H, 4.36; N, 13.78. Fouud: C, 42.99; H, 4.42; N, 13.50.

Registry No.—**1a,** 2140-25-2; **1b,** 40601-48-7; **3a,** 40601-49-8; **3b,** 40601-50-1; **4a,** 40601-51-2; **4b,** 40601-52-3; **5,** 40601-53-4; **6,** 40601-54-5; **7,** 40620-79-9; **8,** 40601-55-6; **9,** 40620-80-2; **10** (R = H), 40620-81-3; **10** (R = CHO), 40620-82-4; **11,** 40620-83-5; **12,** 40620-84-6; tosyl chloride, 98-59-9; adenosine, 58-61-7; mesyl chloride, 124-63-0; sodium benzoate, 532-32-1; 5′-*O*-benzoyl-2′,3′-*O*-isopropylidineinosine, 40582-67-0.