Nucleic Acid Related Compounds. 11. Adenosine 2′,3′-*ribo*-Epoxide. Synthesis, Intramolecular Degradation, and Transformation into 3′-Substituted Xylofuranosyl Nucleosides and the *lyxo*-Epoxide[1,2]

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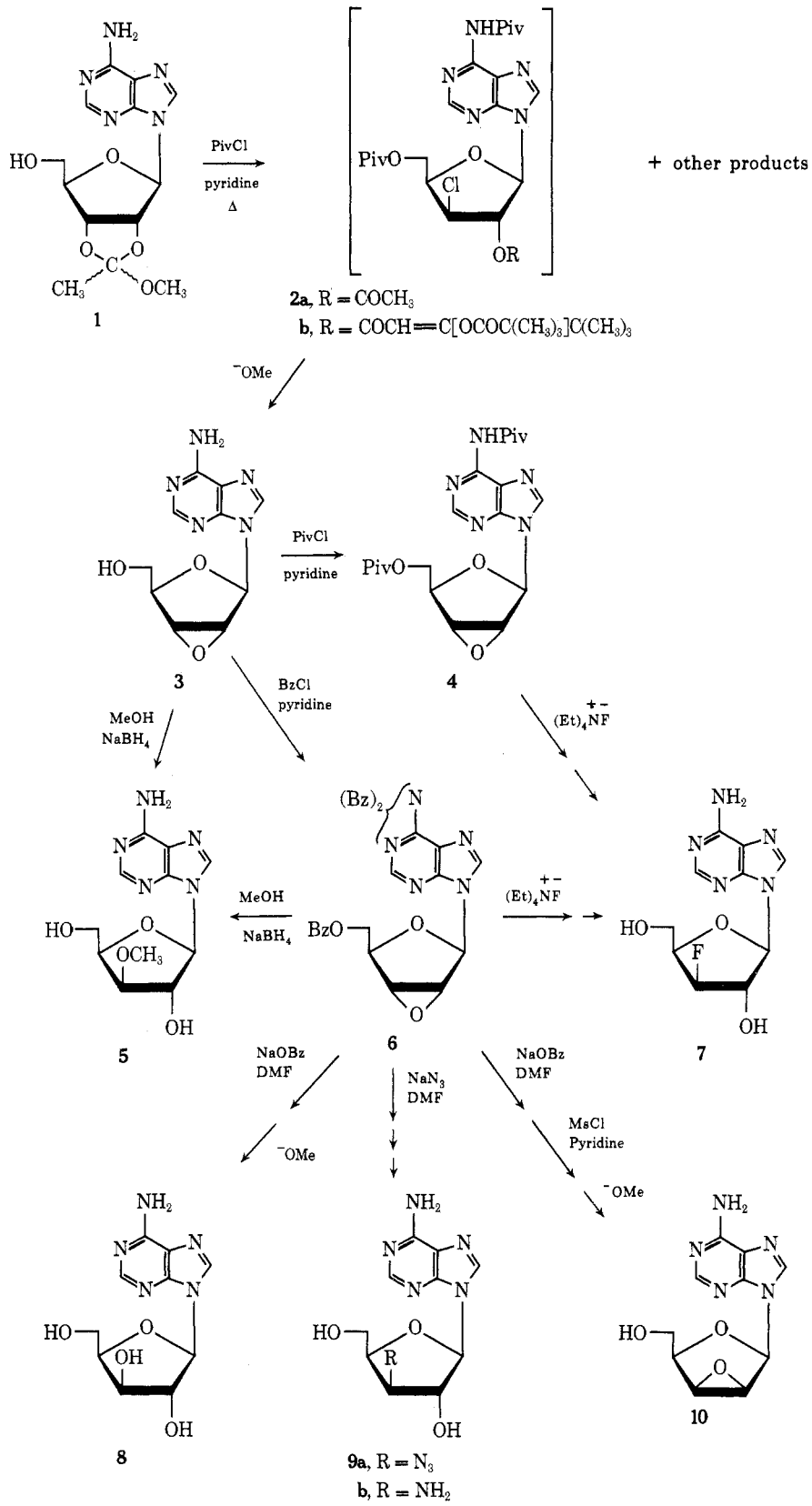
Treatment of 2′,3′-*O*-methoxyethylideneadenosine (1) with excess pivalic acid chloride in refluxing pyridine gave a mixture composed primarily of 6-*N*-pivalamido-9-(3-chloro-3-deoxy-2-*O*-acetyl-5-*O*-pivalyl-β-D-xylofuranosyl)purine (**2a**) and 6-*N*-pivalamido-9-(3-chloro-3-deoxy-5-*O*-pivalyl-2-*O*-[4,4-dimethyl-3-pivalyloxypent-2-enoyl]-β-D-xylofuranosyl)purine (**2b**) in high combined yield. Methanolic sodium methoxide converted this mixture to 9-(2,3-anhydro-β-D-ribofuranosyl)adenine (adenosine *ribo*-epoxide) (**3**) in greater than 60% overall yield from starting adenosine. The epoxide **3** was found to spontaneously decompose (presumably *via* the $N^3 \rightarrow 3'$-*xylo*-cyclonucleoside, i) to the ring-opened aminoimidazole carboxamidine cyclonucleoside ii in water. Sodium hydroxide smoothly effected transformation of ii to the corresponding carboxamide, iii. Pivalylation and benzoylation of **3** in pyridine with the appropriate acid chloride gave 6-*N*-pivalamido-9-(5-*O*-pivalyl-2,3-anhydro-β-D-ribofuranosyl)purine (**4**) and the corresponding $N,N,O^{5'}$-tribenzoate, **6**, respectively. Tetraethylammonium fluoride in refluxing acetonitrile followed by methoxide deblocking converted **4** or **6** into 9-(3-fluoro-3-deoxy-β-D-xylofuranosyl)adenine (**7**). Reaction of **6** with sodium benzoate in moist DMF followed by deblocking gave 9-β-D-xylofuranosyladenine (adenine xyloside) (**8**) in high yield. Treatment of **6** with sodium azide in hot DMF gave 9-(3-azido-3-deoxy-β-D-xylofuranosyl)adenine (**9a**) in excellent yield after removal of protecting groups. Hydrogenation of **9a** gave 9-(3-amino-3-deoxy-β-D-xylofuranosyl)adenine (**9b**). Treatment of the crude product [presumably a mixture of N-benzoylated 9-(3,5-di-*O*-benzoyl-β-D-xylofuranosyl)adenines] from sodium benzoate reaction with **6** with methanesulfonyl chloride in pyridine gave a monomesyl ester. This material was converted into 9-(2,3-anhydro-β-D-lyxofuranosyl)adenine (**10**) upon stirring with methanolic sodium methoxide. Sodium borohydride in methanol effected epoxide ring opening of **6** by methoxide. Treatment of the unblocked epoxide **3** with sodium borohydride in refluxing methanol gave high yields of 9-(3-*O*-methyl-β-D-xylofuranosyl)adenine (**5**) directly with no apparent formation of cyclonucleoside products.

Epoxides are useful intermediates for the introduction of trans β-hydroxy functionality, and various anhydro ring openings have been explored in carbohydrate and nucleoside chemistry.[4] However, adenine nucleoside epoxides had previously been somewhat difficultly accessible by coupling of suitably substituted and stereochemically oriented sugar derivatives with the base followed by subsequent anhydro-forming transformations.[5-8] Certain attempted nucleophilic openings of such *ribo*-epoxides have been unsuccessful owing to N^3 intramolecular attack leading to presumed $N^3 \rightarrow 3'$-cyclonucleosides[7,9] (however, see ref 5, 6, and 9 for successful displacements). We wish to report a convenient and direct synthetic route to *ribo*-epoxides from the corresponding ribonucleosides, preliminary results on their intramolecular degradation, and their transformation into 3′-substituted *xylo*-nucleosides.

Treatment of 2′,3′-*O*-methoxyethylideneadenosine[10,11] (1) with excess pivalic acid chloride in refluxing pyridine gave a mixture composed primarily of 6-*N*-pivalamido-9-(3-chloro-3-deoxy-2-*O*-acetyl-5-*O*-pivalyl-β-D-xylofuranosyl)purine[11,12] (**2a**) and 6-*N*-pivalamido-9-(3-chloro-3-deoxy-5-*O*-pivalyl-2-*O*-[4,4-dimethyl-3-pivalyloxypent-2-enoyl]-β-D-xylofuranosyl)purine[11,12] (**2b**). The crude mixture was treated with methanolic sodium methoxide at room temperature to give 9-(2,3-anhydro-β-D-ribofuranosyl)adenine[5,6,13,14] (**3**) in 63% overall yield from 1. A small amount of contaminating 9-(2-chloro-2-deoxy-β-D-arabinofuranosyl)adenine[11,13,14] was separated from **3** using the useful Dowex 1-X2 (OH^-) column procedure devised by Dekker.[15] This compound is converted into **3** upon more vigorous treatment with base[13,14] than required for the 3′-chloro isomer.

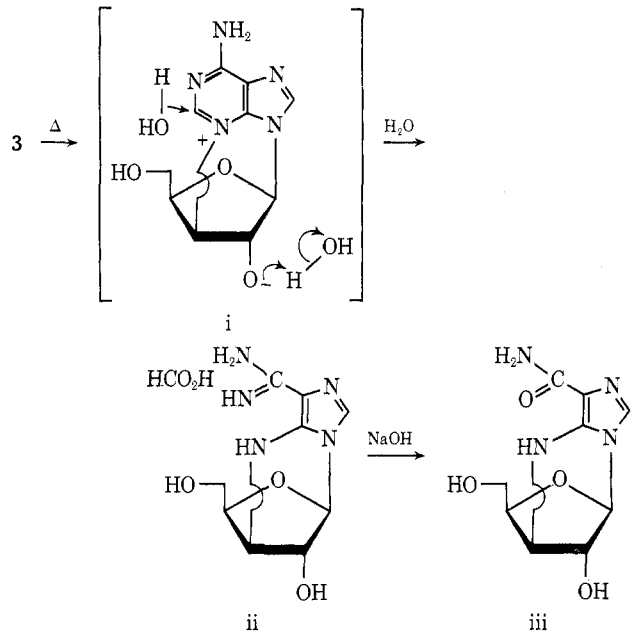
Epoxide **3**, which has been prepared from adenosine by a recently reported[14] alternative procedure, had properties generally consistent with recorded values.[5,6,14] Its melting–decomposition range depends on the rate of heating and its ^1H nmr spectrum has $J_{1'-2'}$ and $J_{3'-4'} \cong 0$.[14] However, it is susceptible to purine ring opening, presumably *via* the $N^3 \rightarrow 3'$-cyclonucleoside i, especially in aqueous solution. In water at room temperature, degradation occurs slowly, but at 80° decomposition is essentially complete after 4 hr (see Figure 1 for a uv absorption *vs.* time study at pH 7). Goodman and coworkers have noted the formation of water-soluble products in reactions of adenine nucleosides involving 2′,3′-*ribo*-epoxides[7,9] and episulfonium[16] intermediates. They postulated $N^3 \rightarrow 3'$-cyclonucleoside structures analogous to **i** on the basis of salt-like properties and a bathochromic shift in the uv absorption maximum. It should be noted, however, that the shift observed in going from the nucleoside (~260 nm) to the postulated $N^3 \rightarrow 3'$-cyclonucleosides[7,9,16] (~293 nm) is 33 nm, whereas a shift of about 12 nm to ~272 nm is ordinarily found with known adenine $N^3 \rightarrow 5'$-cyclonucleosides.[17] The uv maxima of the postulated $N^3 \rightarrow 3'$-cyclonucleosides[7,9,16] at ~293 nm is in reasonable agreement with that of a $N^3 \rightarrow 5'$-cyclonucleoside in the puromycin aminonucleoside series (288 nm).[18] However, the 6-*N*,*N*-dimethylaminopurine nucleoside precursor in that case[18] had its uv maximum at 275 nm, which again corresponds to a 13-nm shift. Uv absorption in the 280–290-nm range has been reported for 5-aminoimidazole-4-carboxamidine.[19,20] It is also of interest that, whereas the $N^3 \rightarrow 5'$-cyclonucleoside of the puromycin aminonucleoside derivative had a negative optical rotation,[18] the derived product of pyrimidine ring opening, 5-amino-1-(3-amino-3-deoxy-2, 3-carbonyl-β-D-ribofuranosyl)imidazole-4-carboxamide $N^5 \rightarrow 5'$-cyclonucleoside[18,20] had a large positive rotation.

The initial product *isolated* from the decomposition of **3** in boiling water had spectral properties in accord with the long-wavelength material of Figure 1. The compound was finally crystallized using ether diffusion into methanol (see Experimental Section) and had elemental analyses compatible with **3** plus two molecules of water. It was strongly basic (spectrophotometrically estimated $pK_a \cong 11.5$), migrated toward the cathode during electrophoresis, had a large positive optical rotation and circular di-



chroism spectrum similar to that of the carboxamide iii, and gave a mass spectral peak at *m/e* 239 as the highest mass peak. These properties are in accord with the structure ii, 5-amino-1-3-deoxy-β-D-xylofuranosyl)imidazole-4-carboxamidine $N^5 \rightarrow 3'$-cyclonucleoside hydroformate salt,[20a] which would be expected to vaporize as the free base in the mass spectrometer. Attack of water on the positively polarized C^2 of the initially formed $N^3 \rightarrow 3'$-cyclonucleoside intermediate, i, followed by hydrolysis of the resulting ring-opened N^5-formyl derivative in the hot aqueous solution, could lead to ii.

Treatment of this solution with sodium hydroxide resulted in a uv spectral shift to 274 nm, which is compatible[18-20] with conversion of ii into 5-amino-1-(3-deoxy-β-D-xylofuranosyl)imidazole-4-carboxamide $N^5 \rightarrow 3'$-cyclonucleoside (iii). Structure iii is supported by elemental analysis, mass spectroscopy (M^+ *m/e* 240), spectrophotometrically estimated pK_a = 2.76, uv absorption,[18,19] and ^1H



nmr spectroscopy. Irradiation of the peak corresponding to H_3' caused the H_2' multiplet to collapse into a doublet ($J_{2'\text{-}2'\text{-OH}}$ = 3.2, $J_{2'\text{-}1'} \cong 0$ Hz) and the N^5-H doublet to collapse into a singlet. Further double-resonance experiments verified the peak assignments and thus, $C^{3'}$-N^5 D-xylofuranosyl)imidazole-4-carboxamide $N^5 \rightarrow 3'$-cyclonucleosides is now placed on a firm experimental basis.[21a] A detailed study of the intramolecular decomposition of various nucleoside epoxides and investigation of products formed will be reported separately.[21b]

An additional point concerning the epoxide **3** *per se* is its optical activity. Goodman and coworkers reported $[\alpha]^{26}D$ −18.3° (*c* 0.6, 20% aqueous pyridine) for a solid which had "several trace spots as contaminants."[6] They recorded $[\alpha]^{26}D$ −17.5° (*c* 0.4, 20% aqueous pyridine) and $[\alpha]^{26}D$ −35.2° (*c* 0.33, H_2O) for an analytical sample (see footnote 11 in ref 6). Moffatt and coworkers[14] report $[\alpha]^{23}D$ −21.8° (*c* 0.2, H_2O) and quoted the $[\alpha]D$ −18.3° value, with no concentration nor solvent specified, from ref 6. A carefully purified and dried sample of **3**, which had no observable cyclonucleoside breakdown products nor other impurities when applied heavily to a tlc plate, had $[\alpha]^{24}D$ −35.4° (*c* 0.22, H_2O) and −20.4° (*c* 0.4, 20% aqueous pyridine) in close agreement with Goodman's values.[6] Considerable care must be exercised in working with **3**, especially in aqueous solutions, since decomposition to highly dextrorotatory products occurs.

Owing to the instability observed with **3**, adenine ring-acylated derivatives were prepared. Jahn[22] has reported that such N-acylated adenosine 5′-tosylates were effective substrates for nucleophilic displacement reactions whereas the unprotected nucleoside readily forms $N^3 \rightarrow 5'$-cyclonucleoside under those conditions. Treatment of **3** with pivalic acid chloride in pyridine at room temperature gave 6-*N*-pivalamido-9-(5-*O*-pivalyl-2,3-anhydro-β-D-ribofuranosyl)purine (**4**) in essentially quantitative yield. Benzoylation similarly afforded an N,N,O^5-tribenzoyl derivative, **6**. Bis-N-benzoylation has usually been assigned N^1,N^6-dibenzoyl structures[23] after the suggestion of Khorana;[23a] however, the N^6,N^6-dibenzoyl isomer was postulated recently.[24]

Treatment of either **4** or **6** with tetraethylammonium fluoride in dry acetonitrile at reflux for an extended period effected epoxide ring opening by fluoride. After deblocking and purification on a Dekker column,[15] 9-(3-fluoro-3-deoxy-β-D-xylofuranosyl)adenine (**7**) was obtained in over 60% yield. Physical properties of **7** were generally in agreement with values reported[25] for a sample prepared by coupling of 2,5-di-*O*-benzoyl-3-fluoro-3-deoxy-α,β-D-xylofuranosyl bromide and 6-benzamidopurine mercury salts. No 2′-fluoro isomer[26] was observed in our sequence of **6** → **7**, although a small amount of 9-β-D-xylofuranosyladenine (**8**) was formed. Tolman and coworkers[27] recently reported obtaining only the product of 3′ attack upon reaction of 9-(2,3-anhydro-β-D-lyxofuranosyl)adenine with KHF_2 in refluxing ethylene glycol.

Sodium benzoate in hot DMF containing some water[28] converted **6** into a presumed mixture of mono- and di-N-benzoylated 9-(3,5-di-*O*-benzoyl-β-D-xylofuranosyl)adenine intermediates which were deblocked to give almost quantitative yields of 9-β-D-xylofuranosyladenine[29] (**8**). Previously recorded physical constants for **8** are rather ill defined.[29] Acid hydrolysis of **8** and paper chromatography[30] of the sugar *vs.* the four aldopentoses showed only xylose present. The ^1H nmr spectrum was in agreement with reported values.[29b,31] The mass spectrum agreed with the tabulation of McCloskey and coworkers.[32] The melting point, ~185° with decomposition, is dependent on how it is heated and previous values[29] differ. The $[\alpha]^{25}D$ −67° (*c* 1.14, H_2O) of **8** is significantly more strongly levorotatory than recorded for other preparations.[29b-d] All of those, however, involved coupling procedures and anomer contamination was possible. This sequence of reactions represents the transformation of a naturally occurring ribonucleoside to its xylo epimer. Such schemes should be applicable to nucleoside antibiotics which are readily accessible by fermentation but which are not practically amenable to base–sugar (or fraudulent sugar) coupling procedures.[33]

Treatment of **6** with sodium azide in hot DMF[34] followed by deblocking gave high yields of 9-(3-azido-3-deoxy-β-D-xylofuranosyl)adenine (**9a**). A trace of presumed 2′-azido isomer was separated by column chromatography[15] and its structure was suggested by the absence of ion d[32] in its mass spectrum, which is characteristic for nucleosides with a 2′-hydroxyl function, as well as other fragmentation effects compatible with the 2′-azido structure. Catalytic hydrogenation of **9a** to give 9-(3-amino-3-deoxy-β-D-xylofuranosyl)adenine (**9b**) proceeded smoothly. This product is seen to be the 3′ epimer of N^6-bis(demethyl)puromycin aminonucleoside.

Treatment of the crude product of reaction of **6** with sodium benzoate–DMF with methanesulfonyl chloride in cold pyridine gave a monomesylate, which was converted to 9-(2,3-anhydro-β-D-lyxofuranosyl)adenine[8] (**10**) by methanolic sodium methoxide. Direct access to this useful[8,35] *lyxo*-epoxide type from naturally occurring ribonucleosides is thus provided.

Reaction of **6** with a large excess of sodium borohydride in methanol proceeded slowly at room temperature to give 9-(3-*O*-methyl-β-D-xylofuranosyl)adenine (**5**) after deblocking. Alternatively, heating **3** in methanol at reflux with sodium borohydride proceeded to give **5** without apparent cyclonucleoside formation. An analogous reaction has been reported very recently[36] in the steroid series. Interestingly, heating a methanolic sodium methoxide solution of **3** at reflux gives but a trace of product migrating (tlc) with **5** plus material not moving from the origin. Inhibitory biological activity of 9-β-D-xylofuranosyladenine (**8**) has been reported[29c,e,37] and the investigation of *O*-methyl ethers of biochemically important nucleosides is of current interest.[38]

The mass spectra of these compounds in general followed trends outlined by McCloskey and coworkers.[32] Certain characteristic fragment ions are listed in Table I. An interesting fragmentation of the epoxides **3** and **10** was

Table I
Characteristic Mass Spectral Ions[a]

Compd	Temp, °C	*m/e* (rel intensity) M	c	d	h	f	b + H	b + 2H	Other selected ions
3	190	249 (4.5)	219 (4.5)		164 (100)	148 (7.5)	135 (85)	136 (48)	202 (2, c − 17), 190 (4.5, j)
5	200	281 (5)	251 (5)	178 (9)	164 (100)	148 (15)	135 (85)	136 (60)	250 (3, M − 31), 220 (7.5, c − 31), 194 (3, i)
7	155	269 (4)	239 (5)	178 (6)	164 (80)	148 (6)	135 (100)	136 (62)	219 (5, c − 20)
8	170	267 (6)	237 (3)	178 (36)	164 (65)	148 (12)	135 (100)	136 (95)	220 (5, c − 17), 194 (6, i), 190 (1.5, j)
9a	120	292 (6)		178 (20)	164 (50)	148 (20)	135 (100)	136 (50)	264 [2, M − 28 (N_2)], 250 [10, M − 42 (N_3)], 220 [30, c − 42 (N_3)]
9b	210	266 (1.5)	236 (4.5)	178 (15)	164 (15)	148 (7.5)	135 (50)	136 (100)	220 (3, c − 16), 194 (32, i)
10	190	249 (5)	219 (6)		164 (100)	148 (10)	135 (45)	136 (45)	202 (1, c − 17), 190 (3, j)

[a] Ions named by letters as in ref 32.

observed, giving an ion corresponding to the loss of 17 mass units (presumably the epoxide oxygen plus a hydrogen) from ion c (M − 30, loss of C5′ as formaldehyde)[32] at *m/e* 202.0721 (calcd for $C_9H_8N_5O$, 202.0729). Neither **3** nor **10** gave a measurable ion d (protonated base plus C1′, C2′, and group attached to C2′)[32] nor ion i (involves transfer of active hydrogen from a heteroatom on C3′). Since ions e and f were postulated[32] to arise from ion d, the reasonably high abundance of ion f in the spectra of **3** and **10** would demand alternate routes. Ion h (protonated adenine plus a formyl group derived from C1′, H1′, and O4′)[32] is seen to be the mass spectral base peak for the two epoxides **3** and **10**. This is of interest since the major pathway previously postulated[32] involves transfer of a hydrogen from the 2′-hydroxyl group in most nucleosides, and ion h was of low intensity in 2′-deoxy derivatives studied where proton transfer from carbon was assumed.[32] The azido nucleoside **9a** undergoes facile loss of the azide function. In fact, no peak corresponding to loss of C5′ as formaldehyde (ion c[32]) was measurable, although a large peak was present at *m/e* 220 (c − N_3). A peak corresponding to loss of the 3′ substitutent (and also a proton in the cases of **3**, **7**, and **10**) from ion c was observed with each of the free nucleosides.

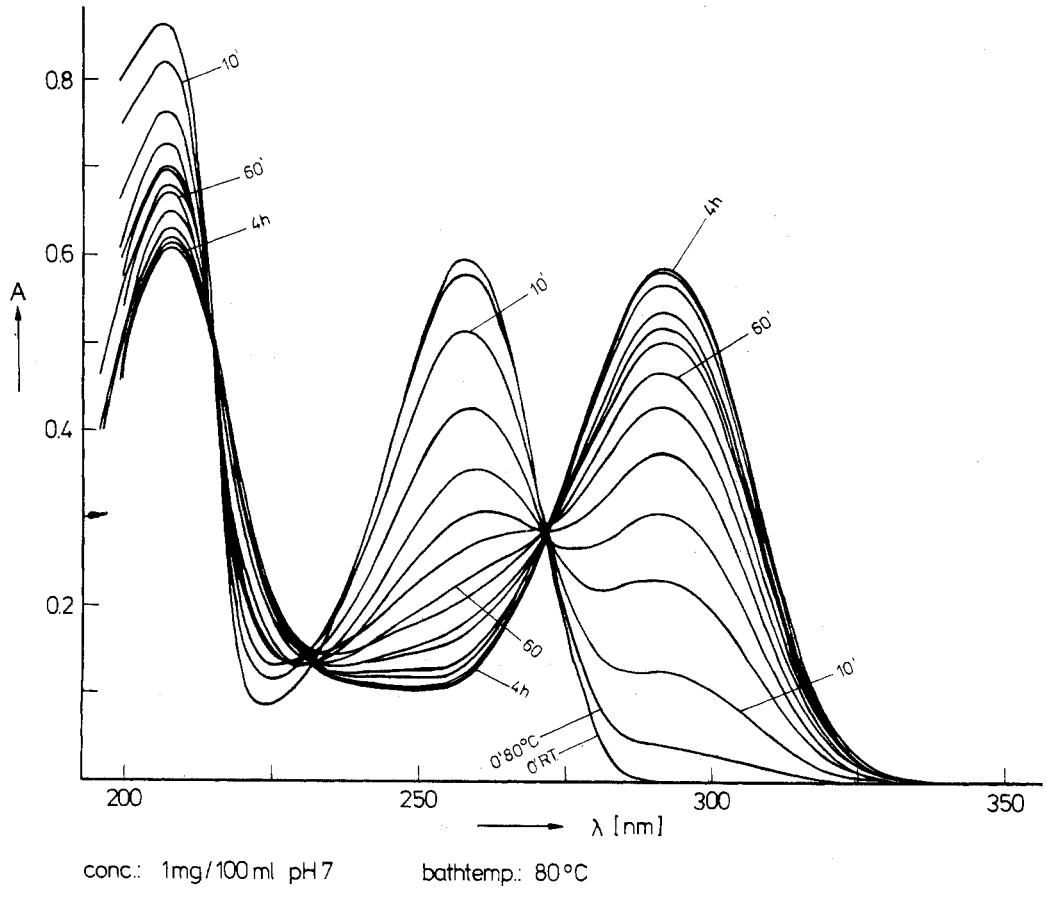


Figure 1. Ultraviolet absorption *vs.* wavelength of a solution of **3** in aqueous solution measured at various times up to 4 hr. No further significant change occurs over at least 10 hr.

This study demonstrates an example of a facile direct conversion of ribonucleosides into their 2',3'-anhydro derivatives and the first generally successful transformation of acylated[39] *ribo*-epoxides into a selected series of xylofuranosyl products and the *lyxo*-epoxide **10**. Studies on other nucleoside epoxides, 2',3'-anhydronucleoside degradations,[21] and further useful synthetic transformations employing nucleoside 2',3'-ortho esters[11,12] will be reported in detail.

Experimental Section

Melting points were determined on a Fisher-Johns apparatus and are uncorrected. Nmr spectra were recorded on Varian 56/60, HA-100, and Bruker 90 spectrometers with TMS or DSS as reference for proton spectra. Uv spectra were recorded on Cary 14 and 15 spectrometers. CD spectra were obtained on a Cary Model 60 instrument. Optical rotations were determined with a Perkin-Elmer Model 141 polarimeter using a 10-cm 1-ml microcell. Mass spectra were determined by the mass spectroscopy laboratory of this department on AEI MS-2 and MS-9 instruments at 70 eV using a direct probe for sample introduction. Elemental analyses were determined by the microanalytical laboratory of this department and Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. Evaporations were effected using Büchler rotating evaporators under aspirator or mechanical oil pump vacuum at 40° or lower. Thin layer chromatography (tlc) was performed on Eastman Kodak chromatogram sheets (silica gel 13181). Column chromatography was effected using J. T. Baker 3405 silica gel.

9-(2,3-Anhydro-β-D-ribofuranosyl)adenine[5,6,13,14] (3). To a solution of 2.9 g (0.009 mol) of 1[10,11] in 60 ml of dry pyridine was added 12 ml (0.1 mol) of pivalic acid chloride dropwise with stirring and exclusion of moisture. The solution was then slowly (1 hr) heated to reflux and refluxed for 1 hr. The resulting yellow solution was allowed to cool to room temperature and 20 ml of MeOH was added dropwise with stirring. This solution was evaporated until precipitation of solid began. Dry Et_2O (100 ml) was added and the mixture was filtered. The filtrate was washed with 2 × 100 ml of 10% $NaHCO_3$ solution and 2 × 100 ml of H_2O, dried over Na_2SO_4, filtered, and evaporated to give a yellow solid foam. This material (composed primarily of **2a** and **2b**)[11,12] was dissolved in 300 ml of MeOH and 3.2 g (0.059 mol) of $NaOCH_3$ was added. The resulting solution was stirred for 17 hr at room temperature, neutralized with HOAc–H_2O (1:9), and evaporated to give a yellow powder. Residual pyridine was removed by codistillation with 3 × 60 ml of dry toluene. The product mixture was partitioned between Et_2O–H_2O (50:20 ml) and the aqueous layer was applied to a column (4 × 40 cm) of Dowex 1-X2 (OH^-) resin packed in MeOH–H_2O (3:7).[15] The column was *rapidly* developed with the same solvent mixture and the appropriate fractions containing pure **3** (tlc) were combined and evaporated to give 1.42 g (63%) of solid **3** after drying. This material had mp ~180° dec (when rapidly heated); $[\alpha]^{24}D$ −35.4° (*c* 0.22, H_2O); uv (H_2O) max 258 nm (ε 14,900), min 225 (2200); uv (0.1 *N* HCl) max 255 nm (ε 14,600), min 228 (3400); uv (0.1 *N* NaOH) max 258 nm (ε 15,000), min 228 (4000); $pK_a \cong 3.55$; nmr (DMSO-d_6) δ 3.58 (m, 2, $H_{5',5''}$), 4.2 ("t", $J_{4'-5',5''} \cong 5$ Hz, 1, $H_{4'}$), 4.25 (d, $J_{3'-2'} = 2.5$ Hz, 1, $H_{3'}$), 4.45 (d, $J_{2'-3'} = 2.5$ Hz, 1, $H_{2'}$), 5.1 (t, 1, 5'-OH), 6.22 (s, 1, $H_{1'}$), 7.26 (s, 2, 6-NH_2), 8.18 (s, 1, H_2), and 8.35 (s, 1, H_8). (See discussion and ref 6 and 14 for literature comparisons.)

Anal. Calcd for $C_{10}H_{11}N_5O_3$: C, 48.19; H, 4.45; N. 28.10. Found: C, 48.43; H, 4.62; N, 28.05.

6-*N*-Pivalamido-9-(5-*O*-pivalyl-2,3-anhydro-β-D-ribofuranosyl)adenine (4). To a suspension of 0.13 g (0.0005 mol) of **3** in 5 ml of dry pyridine was added 0.5 ml (0.004 mol) of freshly distilled pivalic acid chloride and the resulting clear solution was stirred for 28 hr at room temperature. Ice chips were added and the solution was poured slowly with stirring into 150 ml of ice and water. This mixture was extracted with 2 × 150 ml of $CHCl_3$ and the combined organic phase was washed with 2 × 100 ml of 10% aqueous $NaHCO_3$ solution and 2 × 100 ml of H_2O and dried over Na_2SO_4. Drying agent was removed by filtration and the filtrate was evaporated to give 0.21 g (100%) of a pale yellow powder. A more rapidly migrating (tlc) contaminant was readily removed by recrystallization from 95% EtOH to give 0.19 g (92%) of **4**: mp 176–179° dec; uv (MeOH) max 270 nm (ε 18,500), min 230 (3800); nmr (DMSO-d_6) δ 1.0 [s, 9, 5'-OCOC(CH_3)$_3$], 1.28 [s, 9, 6-NHCOC(CH_3)$_3$], 4.0–4.4 (m, 4, $H_{4'}$, $H_{5',5''}$, $H_{3'}$), 4.58 (d, $J_{2'-3'} = 2.5$ Hz, 1, $H_{2'}$), 6.36 (s, 1, $H_{1'}$), 8.60, 8.71 (s, s; 1, 1; H_2, H_8), 10.16 (s, 1, 6-NH-Piv); mass spectrum (175°) *m/e* (rel intensity, ion) 417 (4, M), 332 [16, M − $COC(CH_3)_3$], 316 [4, M − OC-$OC(CH_3)_3$], 220 (16, b + 2), 199 (28, sugar).

Anal. Calcd for $C_{20}H_{27}N_5O_5$: C, 57.53; H, 6.52; N, 16.77. Found: C, 57.35; H, 6.45; N, 16.58.

***N,N*-Dibenzoyl-9-(5-*O*-benzoyl-2,3-anhydro-β-D-ribofuranosyl)adenine (6).** To a suspension of 1.46 g (0.0059 mol) of **3** in 36 ml of dry pyridine was added 3.6 ml (0.031 mol) of freshly distilled benzoyl chloride and the resulting clear solution was stirred for 8 hr at room temperature. Ice chips were added and the solution was poured slowly into 1000 ml of ice and water with vigorous stirring. The resulting white precipitate was filtered, washed with 1000 ml of cold water, and dried (finally *in vacuo* at 78°) to give 2.7 g (82%) of **6**. Recrystallization of 0.2 g of this product from 16 ml of EtOH gave 0.15 g of pure **6**: mp 167–168°; uv (MeOH) max 273, 230 nm (ε 22,600, 35,000), shoulder 250 (27,800); nmr (DMSO-d_6) δ 4.45 (br s, 2, $H_{5',5''}$), 4.6 (m, 2, $H_{3'}$, $H_{4'}$), 4.7 (d, $J_{2'-3'} \cong 3$ Hz, 1, $H_{2'}$), 6.42 (s, 1, $H_{1'}$), 7.3–7.8 (m, 15, aromatic), 8.72, 8.78 (s, s; 1, 1; H_2, H_8); mass spectrum (210°) *m/e* (rel intensity, ion) 561 (25, M), 456 (100, M − COC_6H_5), 440 (37, M − $OCOC_6H_5$), 219 (30, sugar).

Anal. Calcd for $C_{31}H_{23}N_5O_6$: C, 66.30; H, 4.13; N, 12.47. Found: C, 66.08; H, 3.85; N, 12.25.

9-(3-Fluoro-3-deoxy-β-D-xylofuranosyl)adenine[25] (7). To a solution of 0.28 g (0.0005 mol) of **6** in 25 of dry, freshly distilled CH_3CN was added 0.45 g (0.003 mol) of dried tetraethylammonium fluoride. The yellow solution was heated at reflux for 5 days while protected from moisture by a Drierite drying tube and then evaporated. The resulting gum was dissolved in 100 ml of MeOH, 1.0 g (0.019 mol) of sodium methoxide was added, and the solution was stirred for 15 hr at room temperature. This mixture was neutralized with HOAc–H_2O (1:9) and evaporated. The resulting residue was partitioned between 20 ml of Et_2O and 10 ml of H_2O. The aqueous phase was applied to a column (2.2 × 17 cm) of Dowex 1-X2 (OH^-) resin packed in MeOH–H_2O (3:7) and elution was begun with the same solvent mixture. A small quantity (27 mg) of material indistinguishable from 9-β-D-xylofuranosyladenine (**8**) by nmr and mass spectroscopy was obtained, and after changing to MeOH–H_2O (6:4), the desired product, **7**, was eluted. Evaporation of appropriate fractions and crystallization of the residue from 95% EtOH gave 0.085 g (63%) of **7**: mp 212–214°; $[\alpha]^{24}D$ −30.4° (*c* 0.64, DMF) [lit. mp 218–220°; $[\alpha]^{21}D$ −40.1° (*c* 0.5, H_2O); our product was insoluble in H_2O at half this attempted concentration]; uv (0.1 *N* HCl) max 256 nm (ε 14,100), min 228 (4300); uv (H_2O) max 258 nm (ε 14,100), min 223 (2800); uv (0.1 *N* NaOH) max 258 nm (ε 14,300), min 228 (4000); ^1H nmr (DMSO-d_6) δ 3.85 ("d," 2, $H_{5',5''}$), 4.36 (d of sextets, $J_{4'-3'-F} = 28$ Hz, $J_{4'-5',5''} \cong 5.5$ Hz, $J_{4'-3'} \cong 2.5$ Hz, 1, $H_{4'}$), 4.78 (d of t, $J_{2'-3'-F} = 16$, $J_{2'-3'} \cong J_{2'-1} = 2.3$ Hz, 1, $H_{2'}$), 5.1 ("t," $J_{5'-OH-5',5''} \cong 6$ Hz, 1, 5'-OH, 5.13 (d of "t," $J_{3'-3'-F(gem)} = 54$, $J_{3'-2'} \cong 2.3$, $J_{3'-4'} \cong 2.5$ Hz, 1, $H_{3'}$), 6.04 (d, $J_{1'-2'} = 2.3$ Hz, 1, $H_{1'}$), 6.25 (br s, 1, 2'-OH), 7.36 (s, 2, 6-NH_2), 8.14, 8.22 (s, s; 1, 1; H_2, H_8); ^{19}F nmr (DMSO-d_6, ppm upfield, CCl_3F external) δ 200.8 ["octet" (d of d of d), $J_{3'-F-3'(gem)} = 55$, $J_{3'-F-4'} = 28.5$, $J_{3'-F-2'} = 15.5$ Hz, 1, $F_{3'}$].

Anal. Calcd for $C_{10}H_{12}FN_5O_3$: C, 44.61; H, 4.45; F, 7.06; N, 26.01. Found: C, 44.68; H, 4.52; F, 7.03; N, 26.20.

9-β-D-Xylofuranosyladenine[29] (8). To a solution of 0.56 g (0.001 mol) of **6** in 50 ml of DMF containing 2 ml of water was added 0.3 g (0.002 mol) of sodium benzoate. This mixture was heated at 100° for 22 hr with stirring and then evaporated *in vacuo*. The resulting gum was partitioned between 100 ml of $CHCl_3$ and 50 ml of H_2O. The aqueous phase was extracted with 2 × 50 ml of $CHCl_3$ and the combined organic phase was washed with 2 × 100 ml of H_2O, dried over Na_2SO_4, filtered, and evaporated to give a pale yellow, solid foam.

This foam was dissolved in 100 ml of MeOH and 1 g (0.019 mol) of NaOMe was added. The solution was stirred for 16 hr at room temperature, neutralized with HOAc–H_2O (1:9), and evaporated. The residue was partitioned between 20 ml of H_2O and 50 ml of Et_2O and the aqueous phase was applied to a column (2.2 × 20 cm) of Dowex 1-X2 (OH^-) resin packed in MeOH–H_2O (3:7). Elution with the same solvent mixture and evaporation of appropriate fractions gave 0.26 g (100%) of **8**, which could be recrystallized from 95% EtOH to give 0.21 g (80%) of **8**: mp 185–187° dec; $[\alpha]^{25}D$ −67° (*c* 1.14, H_2O) [lit. mp 125–140°,[29a] 225–230°,[29b] 100–130°;[29c] $[\alpha]^{24}D$ −22.5° (*c* 1.22, H_2O),[29f] −16.4° (*c* 1.10, H_2O),[29b] −30.1° (*c* 1.2, H_2O),[29c] −19° (*c* 1.2, H_2O)[29d]]; uv (0.1 *N* HCl) max 255 nm (ε 15,000), min 228 (4000); uv (H_2O) max 258 nm (ε 15,100), min 225 (2400); uv (0.1 *N* NaOH) max 258 nm (ε 15,700), min 225 (3600); nmr (DMSO-d_6) δ 3.7 (m, 2, $H_{5',5''}$), 4.15 (m, 2, $H_{3'}$, $H_{4'}$), 4.35 (m, 1, $H_{2'}$), 4.72 (t, $J_{5'-OH-5',5''} = 6$ Hz, 1, 5'-OH), 5.78 (br s, 1, 3'-OH), 5.83 (br s, 1, 2'-OH), 5.85 [d, $J_{1'-2'} = 2$ Hz

(by D_2O exchange), 1, $H_{1'}$], 7.3 (s, 2, 6-NH_2), 8.15 (s, 1, H_2), 8.3 (s, 1, H_8).

Anal. Calcd for $C_{10}H_{13}N_5O_4$: C, 44.94; H, 4.90; N, 26.20. Found: C, 44.95; H, 4.96; N, 26.33.

9-(2,3-Anhydro-β-D-lyxofuranosyl)adenine[8,40] (10). The procedure given above for the preparation of **8** was followed to the end of the first paragraph. The resulting pale yellow solid foam was dissolved in 50 ml of dry, freshly distilled pyridine and cooled to 0°. Freshly distilled methanesulfonyl chloride (0.1 ml, 0.0013 mol) was added and the solution was stirred for 3 days at 0°. Ice chips were added and the solution was poured into 100 ml of ice water. This mixture was extracted with 150 ml of $CHCl_3$. The organic phase was washed with 100 ml of 10% aqueous $NaHCO_3$ solution and 100 ml of H_2O, dried over Na_2SO_4, filtered, and evaporated. The resulting residue was dissolved in 70 ml of MeOH and the solution was stirred with 0.4 g (0.0075 mol) of NaOMe for 16 hr at room temperature. This solution was neutralized with HOAc–H_2O (1:9) and 2.3 g of neutral silica gel was added. The mixture was evaporated to dryness and the impregnated powder was added to a column (2 × 28 cm, 47 g) of silica gel. The column was washed with EtOAc and the wash was discarded. The product was eluted using EtOAc–MeOH (8:2) and evaporation of appropriate fractions gave a yellow powder, which was crystallized from a mixture of 95% EtOH and *n*-pentane to give 0.126 g (50%) of **10:** mp 208–210° dec; $[\alpha]^{25}D$ −17.5° (*c* 0.19, H_2O) [lit.[40] mp 210–211°; $[\alpha]^{22}D$ −14° (*c* 1, H_2O)]; uv (0.1 *N* HCl) max 258 nm (ε 14,700), min 228 (2600); uv (H_2O) max 258 nm (ε 14,800), min 225 (2000); uv (0.1 *N* NaOH) max 258 nm (ε 14,600), min 225 (2500); nmr (DMSO-d_6) δ 3.6 (m, 2, $H_{5',5''}$), 4.14 (m, 2, $H_{3'}$, $H_{4'}$), 4.25 (d, $J_{2'-3'} \cong 3$ Hz, 1, $H_{2'}$), 5.0 (br s, 1, 5′-OH), 6.26 (s, 1, $H_{1'}$), 7.32 (s, 2, 6-NH_2), 8.18, 8.22 (s, s; 1, 1; H_2, H_8).

Anal. Calcd for $C_{10}H_{11}N_5O_3$: C, 48.19; H, 4.45; N, 28.10. Found: C, 47.95; H, 4.76; N, 28.19.

9-(3-Azido-3-deoxy-β-D-xylofuranosyl)adenine (9a). To a solution of 1.11 g (0.002 mol) of **6** in 100 ml of dry, distilled DMF was added 1 g (0.015 mol) of sodium azide. The mixture was heated for 10 hr at 100° with stirring and then evaporated *in vacuo*. The resulting pale yellow gum was partitioned between 100 ml of $CHCl_3$ and 50 ml of H_2O and the aqueous layer was extracted with 2 × 25 ml of $CHCl_3$. The combined organic phase was washed with 2 × 50 ml of H_2O, dried over Na_2SO_4, filtered, and evaporated to give a pale yellow solid foam. This material was dissolved in 100 ml of MeOH and stirred for 21 hr at room temperature with 1 g (0.019 mol) of NaOMe. The solution was neutralized with HOAc–H_2O (1:9) and evaporated. The residue was partitioned between 50 ml of Et_2O and 20 ml of H_2O and the aqueous layer was evaporated to dryness. The residue was crystallized from H_2O to give 0.54 g (92%) of a pale yellow solid. This material was recrystallized from EtOH to give 0.49 g (83%) of **9a:** mp 177–178°; $[\alpha]^{24}D$ −128° (*c* 0.94, MeOH); uv (H_2O) max 260 nm (ε 15,100) min 232 (3000); nmr (DMSO-d_6) δ 3.65 (br s, 2, $H_{5',5''}$), 4.32 (m, 2, $H_{3'}$, $H_{4'}$), 4.8 ("t," $J_{2'-1'} = 6$, $J_{2'-3'} \cong 6$ Hz, 1, $H_{2'}$), 5.4 (br s, 1, 5′-OH), 5.85 (d, $J_{1'-2'} = 6$ Hz, 1, $H_{1'}$), 6.25 (br s, 1, 2′-OH), 7.35 (s, 2, 6-NH_2), 8.18 (s, 1, H_2), 8.3 (s, 1, H_8).

Anal. Calcd for $C_{10}H_{12}N_8O_3$: C, 41.09; H, 4.14, N, 38.34. Found: C, 41.35; H, 4.27; N, 38.54.

9-(3-Amino-3-deoxy-β-D-xylofuranosyl)adenine (9b). A solution of 0.37 g (0.0013 mol) of **9a** in 100 ml of 95% EtOH was hydrogenated at 45 psi (gauge pressure) for 48 hr at ambient temperature over 0.19 g of 5% Pd/C catalyst. The mixture was filtered, the filter cake was washed with 20 ml of hot EtOH, and the combined filtrate was evaporated to give a white solid which was recrystallized from 95% EtOH to give 0.27 g (81%) of **9b:** mp 250–251°; $[\alpha]^{24}D$ −30.1° (*c* 0.5, H_2O); uv (0.1 *N* HCl) max 255 nm (ε 14,500), min 225 (2500); uv (H_2O) max 258 nm (ε 14,300), min 225 (2000); uv (0.1 *N* NaOH) max 258 nm (ε 14,000), min 228 (3000); nmr (DMSO-d_6) δ 1.1 (t, $J = 7$ Hz, 3, CH_3CH_2OH), 1.8 (br s, 2, 3′-NH_2), 3.3–3.5 (m, 2, $H_{3'}$ and OH), 3.5 (q, $J = 7$ Hz, 2, CH_3CH_2OH), 3.7 (m, 2, $H_{5',5''}$), 4.16 (m, 1, $H_{4'}$), 4.39 ("t," $J_{2'-1'} \cong J_{2'-3'} \cong 6$ Hz, 1, $H_{2'}$), 5.6–5.74 (br d, $J_{1'-2'} \cong 6$ Hz, 2, $H_{1'}$ and OH), 7.3 (br s, 2, 6-NH_2), 8.16 (s, 1, H_2), 8.48 (s, 1, H_8).

Anal. Calcd for $C_{10}H_{14}N_6O_3 \cdot C_2H_5OH$: C, 46.13; H, 6.45; N, 26.91. Found: C, 45.93; H, 6.32; N, 27.00.

9-(3-*O*-Methyl-β-D-xylofuranosyl)adenine (5). To a suspension of 0.25 g (0.001 mol) of **3** in 50 ml of MeOH was added 1.15 g (0.03 mol) of $NaBH_4$. The mixture was heated for 12 hr at reflux with three further additions of 0.25-g portions of $NaBH_4$ after heating for 1, 4, and 6 hr. The solution was evaporated and the white residue was dissolved in 30 ml of H_2O. This solution was continuously extracted with 100 ml of CH_2Cl_2 for 24 hr and the organic phase was evaporated to give 0.28 g (~100%) of white product. A sample of this material (0.28 g) was purified by chromatography on Dowex 1-X2 (OH^-) using MeOH–H_2O (3:7) as the elution solvent mixture followed by evaporation and recrystallization of the residue from MeOH to give 0.24 g (85%) of **5:** mp 167–168°; $[\alpha]^{24}D$ −60.5° (*c* 0.3, MeOH); uv (0.1 *N* HCl) max 258 nm (ε 14,100), min 230 (3000); uv (H_2O) max 258 nm (ε 14,200), min 225 (2500); uv (0.1 *N* NaOH) max 259 nm (ε 14,400), min 230 (3700); nmr (DMSO-d_6) δ 3.3 (s, 3, 3′-OCH_3), 3.72 (br s, 2, $H_{5',5''}$), 3.80 (m, 1, $H_{3'}$), 4.28 (m, 1, $H_{4'}$), 4.56 ("t," $J_{2'-3'} = 2.5$, $J_{2'-1'} = 2.7$ Hz, $H_{2'}$), 4.86 (br s, 1, 5′-OH), 5.90 (br d, 2, $J_{1'-2'} = 2.7$ Hz, $H_{1'}$, 2′-OH), 7.26 (s, 1, 6 NH_2), 8.12 (s, 1, H_2), 8.18 (s, 1, H_8). The mass spectrum of this product had peaks corresponding to that of 3′-*O*-methyladenosine (with significant intensity variations) and different from that of 2′-*O*-methyladenosine.

Anal. Calcd for $C_{11}H_{15}N_5O_4$: C, 46.97; H, 5.37; N, 24.90. Found: C, 46.98; H, 5.66; N, 24.70.

5-Amino-1-(3-deoxy-β-D-xylofuranosyl)imidazole-4-carboxamidine-N^5→3′-cyclonucleoside Hydroformate (ii). A solution of 0.5 g (0.002 mol) of **3** in 50 ml of H_2O was heated for 1 hr at reflux, cooled, and evaporated to dryness. The colorless residue was dissolved in 55 ml of hot MeOH and this solution was filtered. The flask containing the cooled filtrate was sealed in a desiccator containing 250 ml of Et_2O and allowed to stand at room temperature. After 2 days the resulting crystals were filtered and dried at 100° (0.1 mm) over P_2O_5 for 18 hr to give 0.45 g (79%) of colorless needles of ii: mp 230–232°; $[\alpha]^{23}D$ 155° (*c* 1.1, H_2O); $pK_a \cong 11.5$; uv (1 *N* HCl) max 292 nm (ε 13,100), min 237 (2500); uv (pH 7) max 293 nm (ε 14,500), min 252 (2300); uv (pH 13) max 278, 222 nm (ε 9600, 8400), min 243 (5000); acidification of the pH 13 solution back to pH 6 gave essential reproduction of the pH 7 spectrum, indicating that no hydrolysis of the amidine function had occurred; nmr (DMSO-d_6) δ 3.54 (d, $J_{5',5''-4'} \cong 6.7$ Hz; 2, $H_{5',5''}$), 3.81 (d, $J_{3'-4'} = 2.5$, $J_{3'-2'} < 1$ Hz, 1, $H_{3'}$), 4.35 (sextet, $J_{4'-3'} = 2.5$, $J_{4'-5',5''} \cong 6.7$ Hz, 1, $H_{4'}$), 4.52 (d, $J_{2'-3'} < 1$ Hz, 1, $H_{2'}$), 5.63 (s, 1, $H_{1'}$), 7.42 (s, 1, H_2), 8.45 (s, 1, formate), the NH and OH protons gave broad, integrated absorption with no distinct signals.

Anal. Calcd for $C_9H_{13}N_5O_3 \cdot HCO_2H$: C, 42.10; H, 5.30; N, 24.55. Found: C, 42.04; H, 5.38; N, 24.42.

5-Amino-1-(3-deoxy-β-D-xylofuranosyl)imidazole-4-carboxamide-N^5→3′-cyclonucleoside (iii). A solution of 2.0 g (0.008 mol) of **3** in 400 ml of H_2O was heated for 40 min at reflux and 20 ml of 1 *N* NaOH was added. Refluxing was continued for 2 hr and the solution was cooled. Dowex 50 (H^+) resin was added, the mixture was stirred until neutral and filtered, and the filtrate was evaporated to dryness. The residue was dissolved in 200 ml of hot MeOH, the solution was filtered, and methanolic HCl was added. The resulting precipitate was filtered and dried over P_2O_5 at room temperature to give 1.92 g (81%) of iii hydrochloride hydrate, mp ~180° dec.

Anal. Calcd for $C_9H_{12}N_4O_4 \cdot HCl \cdot H_2O$: C, 36.68; H, 5.13; N, 19.01. Found: C, 36.85; H, 4.60; N, 19.18.

A solution of 1 g (0.0034 mol) of this salt in 50 ml of H_2O was neutralized with Dowex 1-X8 (OH^-). The resin was filtered and the filtrate was evaporated to give 0.8 g (95%) of colorless iii. This product was recrystallized from 40 ml of H_2O–EtOH (1:10) to give 0.5 g (60%) of needles which were dried over P_2O_5 at 120° (0.1 mm) for 18 hr to provide iii: mp 234–235°; $[\alpha]^{23}D$ 140° (*c* 1, H_2O); $pK_a \cong 2.76$; uv (1 *N* HCl) max 274; 257 nm (ε 10,600, 10,100), min 263, 223 nm (ε 10,000, 2100); uv (pH 7) max 275 nm (ε 13,800), min 221 (2200); uv (pH 13) max 279 nm (ε 13,400), min 230 nm (3200); nmr (DMSO-d_6–Me_2CO-d_6, 4:1) δ 3.56 (m, 2, $H_{5',5''}$), 3.75 (m, 1, $H_{3'}$), 4.31 ("sextet" $J_{4'-3'} \cong 3.2$, $J_{4'-5',5''} \cong 6.6$ Hz, 1, $H_{4'}$), 4.52 (m, 1, $H_{2'}$), 4.76 ("t," $J_{5'\text{-OH}-5',5''} \cong 6.2$ Hz, 1, 5′-OH), 5.60 (s, 1, H_1), 5.98 (d, $J_{2'\text{-OH}-2'} = 3.2$ Hz, 1, 2′-OH), 6.48 (d, $J_{5\text{-NH}-3'} = 4.4$ Hz, 1, 5-NH), 6.73 (s, 2, $-NH_2$), 7.13 (s, 1, H_2). Irradiation at δ 3.56 ($H_{5',5''}$), caused the exchangeable "triplet" at δ 4.76 (5′-OH) to collapse to a singlet and the "sextet" at δ 4.31 ($H_{4'}$) to collapse to a doublet. Irradiation of the multiplet at δ 3.75 ($H_{3'}$) caused the multiplet at δ 4.52 ($H_{2'}$) to collapse to a clean doublet and the doublet at δ 6.48 (5-NH) to collapse to a singlet. Irradiation at δ 4.52 ($H_{2'}$) caused the multiplet at δ 3.75 ($H_{3'}$) to collapse to a "triplet" and the doublet at δ 5.98 (2′-OH) to collapse to a singlet. These experiments verified the peak assignments and also allowed the determination of $J_{2'-2'\text{OH}} = 3.2$, $J_{2'-3'} \cong 1.2$, and $J_{1'-2'} < 0.7$ Hz.

Anal. Calcd for $C_9H_{12}N_4O_4$: C, 45.00; H, 5.04; N, 23.32. Found: C, 44.93; H, 5.25; N, 23.46.

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Registry No.—ii, 51022-59-4; iii, 51022-60-7; iii hydrochloride, 51096-70-9; **1**, 16667-61-1; **3**, 2627-64-7; **4**, 51014-72-3; **5**, 51014-73-4; **6**, 51014-74-5; **7**, 20535-16-4; **8**, 524-69-6; **9a**, 51014-75-6; **9b**, 51014-76-7; **10**, 40110-98-3.

References and Notes

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(20) In these papers, the compounds are named as 4-aminoimidazole-5-carboxamidines (or carboxamides).
(20a) Note Added in Proof. An X-ray crystallographic analysis of this product is in agreement with the assigned structure. The formic acid molecule is associated with the basic amidine function as would be expected. (Dr. M. N. G. James, Department of Biochemistry, private communication.)
(21) (a) Intermediate formation of the corresponding $N^3 \rightarrow 2'$-arabinocyclonucleoside from **3**, which would have been ring opened to give 5-amino-1-(2-deoxy-β-D-arabinofuranosyl)imidazole-4-carboxamide-$N^5 \rightarrow 2'$-cyclonucleoside instead of iii, was suggested by a referee on the basis of inspection of models. This possibility is precluded by the absence of coupling ($J_{1'-2'} < 0.7$ Hz) of the anomeric proton of iii (and ii), which demands a trans 1′,2′-proton geometry (see ref 31, pp 330–331), as well as by the double-irradiation experiments (*i.e.*, triplet and doublet patterns for the 3′ and 2′ protons upon irradiation of the 2′ and 3′ frequencies, respectively) outlined in the Experimental Section. (b) R. Mengel, *et al.*, in preparation.
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A Solvolytic Investigation of Cyclobutylcarbinyl and Related *p*-Bromobenzenesulfonates

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The solvolysis rates of cyclobutylcarbinyl (**4**-OBs), cyclopentylcarbinyl (**5**-OBs), cyclohexylcarbinyl (**6**-OBs), and 1-adamantylcarbinyl (AC-OBs) brosylates have been determined in a series of solvents. The extent of rearrangement of **5**-OBs is sensitive to reaction conditions, including buffer. The kinetic and product distribution data indicate that solvent capture of a carbon-bridged species accounts for 99% of the acetolysis product of **4**-OBs, 91% of **5**-OBs, and 0% of **6**-OBs.

The occurrence of Wagner–Meerwein type rearrangements in solvolysis reactions of cycloalkylcarbinyl derivatives has been well demonstrated.[2] To the extent that the current view of solvolysis reactions[3] is correct, the observation of Wagner–Meerwein type rearrangement products in the solvolysis of cycloalkylcarbinyl arenesulfonates is evidence for neighboring group participation in the ionization step *via* σ-bond delocalization of charge into the cycloalkane ring.

Although the study of the nature of σ-bond participation by the cyclopropane ring in solvolysis reactions has been the subject of considerable experimental and theo-