S, 10.75; mol wt, 298. Found: C, 52.15; H, 6.04; N, 9.22; S, 10.98; mol wt, 298 (mass spectrum).

1-(2,3-Dideoxy-3,5(*S,O*)-isopropylidene-β-D-*threo*-pentofuranosyl)-3-methylthymine (18).—A solution of **15** (300 mg, 1.0 mmol) in 22 ml of 0.1 *N* sodium hydroxide and 5 ml of methyl iodide was stirred overnight at room temperature. The reaction mixture was evaporated *in vacuo* and the residual syrup triturated with water. This solid was filtered, 160 mg (51%), mp 139–140°. In the pH region of 5.4–12 the ultraviolet absorption maximum was 267 mμ.

Anal. Calcd for $C_{14}H_{20}N_2O_4S$: C, 53.82; H, 6.45; N, 8.97; S, 10.26. Found: C, 53.75; H, 6.41; N, 8.92; S, 10.19.

3'-Deoxythymidine (16).—A suspension of **14** (111 mg, 4.3 mmol) in 10 ml of water was stirred and treated with 1 *N* sodium hydroxide dropwise until complete solution was obtained. Activated Raney nickel (*ca.* 2 ml of thick slurry) was added and the reaction mixture stirred at room temperature for 1 hr. (The optical density at 267 mμ showed a decrease of 43% during this period.) The nickel was filtered and washed well with water. The filtrate was neutralized with dilute acetic acid and the solvent evaporated *in vacuo* to dryness. The residue was reconcentrated three times with ethanol and the resulting white solid triturated several times with boiling acetone. The acetone extracts were combined and evaporated *in vacuo* to a solid. The product (**16**, 36 mg, 37%, mp 145° with sinter at 140°[14]) gave a negative nitroprusside test. The presence of a single product was demonstrated by tlc in system c.

When this reaction was repeated using a much smaller amount of the Raney nickel catalyst, no **16** was formed. The only product was the disulfide **17**, identified by tlc (system c).

Disulfide (17) of Compound 14.—A solution of 100 mg (0.4 mmol) of **14** in 20 ml of 1 *N* sodium hydroxide was aerated for 24 hr. The sodium carbonate was filtered and the filtrate acidified with 1 *N* hydrochloric acid and evaporated to dryness. The residue was recrystallized from hot water. The yield of **17** was 60 mg (59%), mp 252–255°. The infrared spectrum showed the absence of a thiol peak in the 2600-cm^{-1} region: ultraviolet absorption data, $\lambda_{max}^{pH\ 0\text{-}6.34}$ 267 mμ; λ_{min} 235 mμ; $\lambda_{max}^{pH\ 12}$ 212 and 267 mμ, inflection at 225 mμ; λ_{min} 244 mμ; pK_a 9.8 ± 0.05 (spectrophotometrically determined).

Registry No.—**3**, 18634-58-7; **6**, 18634-59-8; **7**, 18634-60-1; **8**, 18634-61-2; **14**, 18634-62-3; **15**, 18634-63-4; **16**, 18634-64-5; **17**, 18634-65-6; **18**, 18634-66-7.

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Purine Nucleosides. XXIII. Direct Amination of Purine Nucleosides[1]

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The direct introduction of an amino group into the purine moiety at positions N-1 and N-7 has been achieved in various purine nucleosides. This is the first reported direct amination of a purine ring nitrogen. Hydroxylamine-O-sulfonic acid converted inosine into 1-aminoinosine (**2**) and guanosine to 1-aminoguanosine (**4**). 6-Amino-9-β-D-ribofuranosyl-8-purinone (**7**) similarly gave 6,7-diamino-9-β-D-ribofuranosyl-8-purinone (**8**). A sequence of stepwise amination procedures with hydroxylamine-O-sulfonic acid provided direct introduction of the amino group at both positions N-1 and N-7 to give 1,2,7-triamino-9-β-D-ribofuranosyl-6,8-purinedione (**12**). These unique nucleoside derivatives provide interesting tools for future biochemical study. Since the N-amino group is capable of acting either as a hydrogen-bond acceptor or donor, these compounds at the nucleotide and polynucleotide level should present unusual possibilities for interaction with protein and nucleic acid.

Although early attempts to prepare certain N-aminopurines were unsuccessful,[2] Montgomery and coworkers prepared 9-N-aminohypoxanthine[3] and 9-amino-6-chloropurine[4,5] by appropriate ring-closure procedures of requisite hydrazinopyrimidine derivatives. Although the synthesis of 9-amino-6-chloro-8-hydroxypurine has been reported by ring closure of 5-amino-4-chloro-6-hydrazinopyrimidine with phosgene,[6] a recent publication[7] has shown this original structural assignment to be in error. The only reported N-amino derivatives of purines where the amino group is attached directly to a ring nitrogen atom are 9-N-aminopurines[3-7] or 9-N-substituted aminopurine derivatives.[5,8] In all instances the N-amino group was introduced into the purine moiety *via* ring-closure procedures of preformed pyrimidine intermediates or in one instance by ring closure of a 1-amino derivative of imidazole.[9]

Of considerable interest would be the synthesis of N-aminopurine nucleosides with an amino group attached at various potentially hydrogen-bonding sites on the heterocyclic base. The amino group is especially attractive for this purpose since this group is capable of acting either as a hydrogen bond acceptor or donor. The 9-N-aminopurines are unsuitable for this study since the position required for nucleoside formation is blocked. Since purine derivatives with an N-amino function on other nitrogen atoms are unknown this problem was viewed from the possibility of *direct* introduction of an amino group into the preformed purine ring of naturally occurring purine nucleosides.

Hoegerle and Erlenmeyer[10] treated 2-pyridone with

(1) This work was supported by Research Grants No. CA-08109-02 and CA-08109-03 from the National Cancer Institute of the National Institutes of Health, Public Health Service.

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(4) C. Temple, Jr., B. H. Smith, Jr., and J. A. Montgomery, *J. Org. Chem.*, **28**, 923 (1963).

(5) C. Temple, Jr., R. L. McKee, and J. A. Montgomery, *ibid.*, **28**, 2257 (1963).

(6) M. H. Krackov and B. E. Christensen, *ibid.*, **28**, 2677 (1963).

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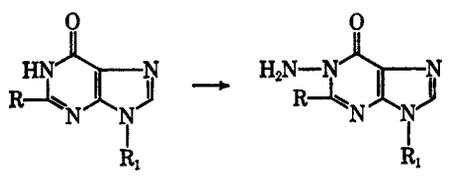
(8) C. L. Leese and G. M. Timmis, *J. Chem. Soc.*, 3818 (1961).

(9) R. N. Naylor, G. Shaw, D. V. Wilson, and D. N. Butler, Jr., *ibid.*, 4845, (1961).

(10) K. Hoegerle and H. Erlenmeyer, *Helv. Chim. Acta*, **39**, 1203 (1956).

chloramine in alkaline solution and obtained 1-amino-2-pyridone in low yield. Recent synthesis of N-aminouracils[11,12] by Klötzer utilizing hydroxylamine-O-sulfonic acid[8,9] suggested the possible use of this reagent to prepare N-aminopurine nucleosides directly. This approach may be viewed as a direct N-amination procedure *via* a positive amino group. Methylation of purine nucleosides has been studied in detail[13–15] and is



1, 3, 5 **2, 4, 6**

1, R = H; R_1 = β-D-ribofuranosyl
2, R = H; R_1 = β-D-ribofuranosyl
3, R = NH_2; R_1 = β-D-ribofuranosyl
4, R = NH_2; R_1 = β-D-ribofuranosyl
5, R = NH_2; R_1 = 2′-deoxy-β-D-ribofuranosyl
6, R = NH_2; R_1 = 2′-deoxy-β-D-ribofuranosyl

a good method of preparing various methylated purine nucleosides found in soluble RNA. Thus in the presence of base it should be possible to remove the proton adjacent to a keto group in the purine ring and introduce an N-amino group much the same as the N-alkylation procedures already reported[13–15] from this laboratory. This indeed proved to be the case. Hydroxylamine-O-sulfonic acid and inosine (**1**) in the presence of sodium hydroxide gave a 65% yield of 1-aminoinosine (**2**). Under similar conditions guanosine (**3**) yielded 1-aminoguanosine (**4**). 2′-Deoxyguanosine (**5**) and hydroxylamine-O-sulfonic acid in 1 *N* sodium hydroxide gave approximately 40% yield of 1-amino-2′-deoxyguanosine (**6**). In each instance the products were separated from a certain amount of starting nucleoside which was soluble in dilute aqueous ammonia.

Examination of the ultraviolet spectra of the various N-amino nucleosides permits definite assignment of the position of methylation. Each of the purine nucleosides listed in Table I possesses spectral characteristics virtually identical with those of the corresponding N-methylpurine nucleosides. Apparently there is no significant delocalization of the lone electron pair on the exocyclic nitrogen. This is also supported by the spectra in acid media. Protonation of the N-amino group does not appreciably alter the chromophoric system. Each of the corresponding N-methylpurine nucleosides has been synthesized in our laboratories[13–16] by standard methylation procedures. The possibility of introducing the amino group at position N-7 was next investigated. 6-Amino-9-β-D-ribofuranosyl-8-purinone (**7**, 8-oxoadenosine) prepared by the method of Holmes and Robins[17] was treated with hydroxylamine-O-sulfonic acid in aqueous base to give 7-amino-8-oxoadenosine (**8**) in 40% yield. The possibility of introducing two N-amino groups into the purine ring was next investigated. 8-Benzyloxyguanosine[17] (**9**) was successfully aminated to 1-amino-8-benzyloxyguanosine (**10**). Palladium on carbon in the presence of hydrogen smoothly removed the benzyl group to give 1,2-diamino-9-β-D-ribofuranosyl-6,8-purinedione (**11**, 1-amino-8-oxoguanosine). Treatment of **11** with hydroxylamine-O-sulfonic acid in the presence of aqueous base gave a 57% yield of 1,2,7-triamino-9-β-D-ribofuranosyl-6,8-purinedione (**12**, 1,7-diamino-8-oxoguanosine) (Scheme I). Assignment of the positions of the N-amino groups was made on the basis of comparison of the ultraviolet (uv) absorption spectra with the corresponding N-methylpurine nucleosides (Table I). An attempt to prepare 1,2,7-triamino-9-β-D-ribofuranosyl-6,8-purinedione (**12**), by direct amination of 8-oxoguanosine in the presence of a 4 molar equiv excess of hydroxylamine-O-sulfonic acid gave, in addition to starting material, approximately equal quantities of 1-amino-8-oxoguanosine (**11**) and the desired product **12**.

It should be pointed out that there are certain differences in the N-methylation and N-amination procedures. It has been shown[13,18] that methylation of

TABLE I

ULTRAVIOLET ABSORPTION SPECTRA OF SOME N-AMINO- AND N-METHYL-PURINE NUCLEOSIDES

No.	Compound	pH 1, λ_{max} ($\epsilon_{max} \times 10^{-3}$)	pH 11, λ_{max} ($\epsilon_{max} \times 10^{-3}$)	MeOH, λ_{max} ($\epsilon_{max} \times 10^{-3}$)	pH 7, λ_{max} ($\epsilon_{max} \times 10^{-3}$)
2	1-Aminoinosine	250 (9.9)	251 (9.9)	251 (9.6)	
				266 (s)	
4	1-Aminoguanosine	257 (11.6)	255 (14.3)	256 (16.4)	
		278 (s[a])	268 (s)	270 (s)	
6	1-Amino-2′-deoxyguanosine	257 (11.8)	254 (14.0)	256 (15.9)	
		279 (s)	267 (s)	270 (s)	
10	1-Amino-8-benzyloxyguanosine	248 (7.7)	251 (9.7)	253 (5.6)	
		294 (6.4)	283 (5.6)	284 (5.6)	
11	1-Amino-8-oxoguanosine	248 (12.1)	259 (12.4)	252 (13.4)	
		294 (10.4)	300 (9.45)	293 (10.3)	
12	1,7-Diamino-8-oxoguanosine	248 (12.3)	252.5 (11.8)		249 (12.3)
		296 (10.4)	297 (10.0)		296 (10.4)
8	7-Amino-8-oxoadenosine	269 (12.2)	273 (13.4)		273 (13.4)

[a] s, singlet.

(11) W. Klötzer and M. Herberz, *Monatsh. Chem.*, **96**, 1731 (1965).
(12) W. Klötzer, *ibid.*, **97**, 1117 (1966).
(13) J. W. Jones and R. K. Robins, *J. Amer. Chem. Soc.*, **85**, 242 (1963).
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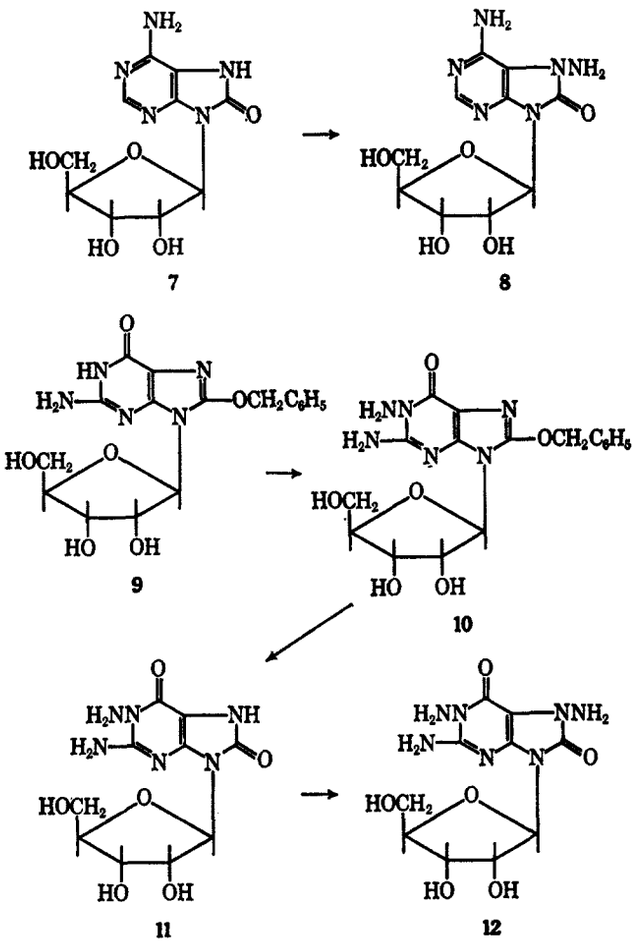
TABLE II

PMR SPECTRA OF SOME N-AMINOPURINE NUCLEOSIDES[a]

No.	Compound	Chemical shifts, δ						
		1-NH_2	2-NH_2	6-NH_2	7-NH_2	H-2	H-8	H-1′
2	1-Aminoinosine	5.97				8.43	8.40	6.02
4	1-Aminoguanosine	5.47	7.18				8.08	5.84
6	1-Amino-2′-deoxyguanosine	5.42	7.12				8.00	6.22
10	1-Amino-8-benzyloxyguanosine	5.48	6.95					5.75
11	1-Amino-8-oxoguanosine	5.37	6.98					5.61
12	1,7-Diamino-8-oxoguanosine	5.38	7.10		5.13			5.68
8	7-Amino-8-oxoadenosine			6.77	5.72	8.08		5.80

[a] All spectra were determined in DMSO-d_6.

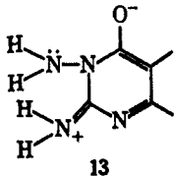
SCHEME I



inosine or guanosine in aqueous base leads to methylation at position 7 followed by rapid hydrolytic cleavage of the imidazole ring to give a pyrimidine derivative. Methylation at position 1 is achieved only in a nonaqueous basic system such as dimethyl sulfoxide–anhydrous potassium carbonate.[15] On the other hand, aminations with hydroxylamine-O-sulfonic acid appear to proceed *only* in aqueous base. All attempts to execute these reactions in nonaqueous solvents gave only starting material.

Treatment of various N-aminouracil derivatives with nitrous acid regenerates the corresponding uracil.[11,12] 1-Aminoinosine (**2**) in glacial acetic acid in the presence of sodium nitrite gave inosine as the only detectable product. Similar deamination of 1-aminoguanosine (**4**) with 1 mol of nitrous acid, under conditions which are known to convert guanosine into xanthosine, gave only guanosine (**3**). This is in sharp contrast to treatment of 2-hydrazinohypoxanthine with nitrous acid which gives an equilibrium of 2-azidohypoxanthine and the two possible N-1 and N-3 tetrazoles.[19] Although the mechanism of this type of deamination is presently not understood it is clear that the unimolecular decomposition of an intermediate diazonium ion cannot occur since this would lead to the formation of an N-oxide.

The proton magnetic resonance (pmr) data for the N-aminopurine nucleosides are given in Table II. The chemical shifts of the N-amino protons are substantially upfield (>1 ppm in all cases studied) from those of the amino groups attached directly to carbon even though nitrogen is more electronegative than carbon. This phenomenon is readily explained as a contribution from the immonium resonance structure **13**. Such a resonance delocalization is obviously not available to the N-amino lone-pair electrons. Consideration of this same resonance form (**13**) also pro-



13

vides a probable explanation for the fact that the N-amino group of 1-aminoinosine (**2**) is deshielded by 0.50 ppm compared with that of 1-aminoguanosine (**4**). Delocalization such as noted in **13** results in a general increase in the basicity of the ring system and a corresponding increase in shielding of the N-amino protons.

Table III shows the effect of N substitution on a nearby substituent attached to carbon. In the series of 2-amino derivatives methylation at position 1 results in a downfield shift of the 2-amino protons of 0.48 ± 0.05 ppm while amination produces a slightly greater downfield shift (0.56±0.06 ppm). Both methylation and amination at the one position of inosine (**1**)

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TABLE III
COMPARISON OF PMR SPECTRA OF CERTAIN N-AMINOPURINE NUCLEOSIDES WITH THE CORRESPONDING N-METHYLPURINE NUCLEOSIDES[a]

	Chemical shift, δ 2-NH₂	$\delta_2 - \delta_1$	$\delta_3 - \delta_1$	$\delta_4 - \delta_2$
Guanosine	6.65			
1-Methyl-[b]	7.09	0.44	0.53	0.09
1-Amino-	7.18			
2′-Deoxyguanosine	6.52			
1-Methyl-[b]	7.05	0.53	0.60	0.07
1-Amino-	7.12			
8-Benzyloxyguanosine	6.48			
1-Methyl-[c]	6.92	0.44	0.48	0.04
1-Amino-	6.96			
8-Oxoguanosine	6.47			
1-Methyl-[c]	6.93	0.46	0.51	0.05
1-Amino-	6.98			
	6-NH₂			
8-Oxoadenosine	6.57			
7-Methyl-[c]	6.73	0.16	0.20	0.04
7-Amino-	6.77			
	2-H			
Inosine	8.27			
1-Methyl-[d]	8.43	0.16	0.16	0.00
1-Amino-	8.43			

[a] All spectra were determined in DMSO-d_6. [b] Reference 14. [c] Reference 16. [d] Reference 13.

results in a downfield shift of H-2 by 0.16 ppm. Substitution at position 7 in 8-oxoadenosine causes a similar paramagnetic shift of the 6-amino group. The paramagnetic shift of H-2 of 1-methylinosine relative to H-2 of inosine has been explained[20] by the proposal of a relatively greater degree of quaternization in 1-methylinosine compared with inosine itself. It would be expected that amination would have the same effect, and indeed it does (Table III). This explanation is not adequate, however, to account for the nearly identical paramagnetic shift of the N-6 protons observed upon substitution at N-7 of 8-oxoadenosine. While in 1-aminoinosine the partial quaternization is occurring on a nitrogen atom attached directly to the carbon bearing the proton undergoing deshielding **8**, in two carbons and a nitrogen intervene between the affected proton and the site of partial quaternization. It has been found[21] that the effect of a substituent on a proton in a 1,3 "diequatorial" position with respect to such a substituent is to deshield the proton. It is now possible to account for much larger effects experienced by the 2-amino group upon 1 substitution. In this case both the quaternization effect and the effect through space of the substituent are working in the same direction and combine to give the large shifts of the amino protons seen in Table III.

The introduction of methyl groups into RNA produces profound alterations in nucleic acid structure. The methyl groups at positions 1 and 7 of the purine nucleotides may give rise to structural changes due to steric or electronic factors or a combination of both and the presence of these groups appear to be very important in the tertiary structure of *t*-RNA.[22] One of these naturally occurring nucleosides, 1-methylguanosine, has been enzymatically incorporated into a homopolymer by Pochon and Michelson.[23] The methyl group is a bulky, hydrophobic structure which probably exerts its influence in nucleic acid largely in a steric fashion. The introduction of an amino group at positions 1 and 7 of the purine nucleosides provides a substituent of comparable size at the same site as the methyl group which should exert a similar steric effect. The amino group, however, is *hydrophilic* in nature instead of hydrophobic. The N-amino group may act in hydrogen bonding either as a donor or acceptor. The present study points the way to the possibility of introducing the *hydrophilic* N-amino group into polynucleotides and nucleic acids either by incorporation or direct amination. The direct amination of certain nucleic acid fractions might be achieved by hydroxylamine-O-sulfonic acid or by the use of other selective positive aminating agents.[24] The placement of the hydrophilic N-amino group in selected sites in the heterocyclic bases could be of major importance in future studies of tertiary structure and hydrogen bonding interactions of nucleic acids.

Experimental Section

Materials and Methods.—Hydroxylamine-O-sulfonic acid was purchased from Alfa Chemical Co., Beverly, Mass. 01915. Uv spectra were determined on a Beckman DK-2 or a Perkin-Elmer 202 spectrophotometer. Pmr spectra were run in DMSO-d_6 (DSS internal standard) on a Varian A-60 or a Varian 56-60 spectrometer. Melting points were measured on a Fisher-Johns apparatus and are uncorrected. Elemental analysis were performed by M-H-W Laboratories, Garden City, Mich. 48135.

1-Aminoinosine (2).—Inosine (**1**, 5.4 g, 20 mmol) was dissolved in 60 ml of 1 *N* sodium hydroxide solution. Hydroxylamine-O-sulfonic acid (3.4 g, 30 mmol) in 40 ml of water was added. The solution was allowed to stand at 2° for 20 hr. The solution was evaporated to dryness *in vacuo*, the solid residue was taken up in about 50 ml of hot water, and the solution was allowed to crystallize at 2° overnight. The white crystals were filtered, washed with cold water, then with acetone, and air dried to give 3.7 g (65%), mp 215–225°, essentially chromatographically homogeneous.[25] The first recrystallization was carried out from dilute ammonium hydroxide to ensure that any unreacted inosine remained in solution. Two additional recrystallizations from water afforded an analytical sample, mp 235–237°.

Anal. Calcd for $C_{10}H_{13}N_5O_5$: C, 42.4; H, 4.60; N, 24.7. Found: C, 42.4; H, 4.70; N, 24.7.

1-Aminoguanosine (4).—Guanosine (**3**, 5.7 g, 20 mmol) was dissolved in 60 ml of 1 *N* sodium hydroxide solution. Hydroxylamine-O-sulfonic acid (3.4 g, 30 mmol) in 40 ml of water was added. The solution was stirred 18 hr at room temperature. The white solid was filtered, washed with water, then acetone, and air dried to give 2.0 g (33%). One recrystallization from dilute ammonium hydroxide followed by one recrystallization from water afforded an analytical sample, mp 270° dec.

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(24) T. Sheradsky, *Tetrahedron. Lett.*, 1909 (1968).

(25) It should be noted that for this and succeeding aminations, unreacted starting material can be recovered simply by neutralizing the reaction mixture with dilute sulfuric acid, cooling the solution to about 5°, and filtration of the solid. This starting material is pure enough to be recycled in the reaction. Since this procedure was not routinely followed, all reported yields are based on total, rather than unrecovered, starting material.

Anal. Calcd for $C_{10}H_{14}N_6O_5$: C, 40.3; H, 4.70; N, 28.2. Found: C, 40.6; H, 4.88; N, 28.0.

1-Amino-8-benzyloxyguanosine (10).—8-Benzyloxyguanosine (**9**, 3.9 g, 10 mmol) was dissolved in 60 ml of 1 *N* sodium hydroxide solution. Hydroxylamine-O-sulfonic acid (3.4 g, 30 mmol) dissolved in 40 ml of water was added. The solution was allowed to stand overnight at room temperature. The white crystals were filtered, washed well with water and acetone, and air dried to give 2.8 g (69%), melting range 221–228°. Two recrystallizations from ethanol–water gave an analytical sample, melting range 230.5–232° dec.

Anal. Calcd for $C_{17}H_{20}N_6O_6$: C, 50.5; H, 4.95; N, 20.85. Found: C, 50.33; H, 4.98; N, 20.89.

1-Amino-8-oxoguanosine (11).—1-Amino-8-benzyloxyguanosine (2.0 g, 5 mmol) was dissolved in a boiling 1:1 mixture of ethanol–water, added to 5% palladium on charcoal (1.0 g), and hydrogenated on a Parr apparatus at 42 psi for 20 hr. The catalyst was filtered and washed with hot water. The filtrate was evaporated to dryness *in vacuo* and crystallized from a small volume of water to give 1.0 g (63%), decomposing above 275°.

Anal. Calcd for $C_{10}H_{14}N_6O_6$: C, 36.8; H, 4.34; N, 25.8. Found: C, 36.9; H, 4.85; N, 25.5.

1-Amino-2′-deoxyguanosine (6).—2′-Deoxyguanosine (**5**, 2.67 g, 10 mmol) was dissolved in 30 ml of 1 *N* sodium hydroxide solution. Hydroxylamine-O-sulfonic acid (1.7 g, 15 mmol) in 20 ml of water was added, and the solution was kept at 2° for 18 hr. The white solid was filtered, washed with cold 1 *N* sodium hydroxide solution, water, and acetone, and then air dried to give 1.1 g (39%). Two recrystallizations from water afforded an analytical sample, mp 239–242°.

Anal. Calcd for $C_{10}H_{14}N_6O_4$: C, 42.5; H, 5.00; N, 29.8. Found: C, 42.2; H, 5.32; N, 29.6.

Deamination of 1-Aminoguanosine.—1-Aminoguanosine (**4**, 0.30 g, 1 mmol) was suspended in glacial acetic acid (3 ml) and treated with sodium nitrite (0.07 g, 1 mmol) dissolved in about 1 ml of water. The mixture was stirred overnight at room temperature. The white precipitate was filtered, washed with water and ethanol, and air dried to give 0.183 g (65%) of guanosine having the correct uv spectrum and chromatographically identical with an authentic sample. The filtrate was shown chromatographically to contain only guanosine and 1-aminoguanosine. No xanthosine was detected.

1,7-Diamino-8-oxoguanosine (12).—1-Amino-8-oxoguanosine (**11**, 1.63 g, 5.2 mmol) was dissolved in 30 ml of 1 *N* sodium hydroxide solution. Hydroxylamine-O-sulfonic acid (1.7 g, 15 mmol) in 20 ml of water was added. The solution was stirred for 3 hr at room temperature, then kept at 2° for 72 hr. The solid was filtered, washed with water, then with acetone, and air dried to give 0.97 g (57%), mp 272–274° dec. A sample was crystallized three times from water containing a few drops of concentrated ammonium hydroxide to give an analytical sample, which darkened at 266° and decomposed at 276–278°.

Anal. Calcd for $C_{10}H_{15}N_7O_6$: C, 36.4; H, 4.56; N, 29.8. Found: C, 36.2; H, 4.47; N, 30.04.

7-Amino-8-oxoadenosine (8).—8-Oxoadenosine[17] (**7**, 1.42 g, 5 mmol) was dissolved in 1 *N* sodium hydroxide solution (25 ml). Hydroxylamine-O-sulfonic acid (1.7 g, 15 mmol) in water (15 ml) was added all at once. The solution was stirred for 4 hr at room temperature, then stored at 2° for 72 hr. The solid was filtered, washed with water and acetone, and air dried to give 0.60 g (40%), mp 256–258° dec. A sample was recrystallized from dilute ammonium hydroxide, then from water, to give white needles, mp 268–269° dec.

Anal. Calcd for $C_{10}H_{14}N_6O_5$: C, 40.3; H, 4.70; N, 28.2. Found: C, 40.3; H, 4.75; N, 28.2.

Registry No.—**2**, 19029-66-4; **4**, 19039-33-9; **6**, 19029-67-5; **8**, 19029-68-6; **10**, 19029-69-7; **11**, 19029-70-0; **12**, 19029-71-1.

Branched-Chain Sugar Nucleosides. I. 9-[3-Deoxy-3-*C*-(2′-hydroxyethyl)-β-D-allofuranosyl]adenine and 9-[3-Deoxy-3-*C*-(2′-hydroxyethyl)-β-D-ribofuranosyl]adenine

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The synthesis of two novel branched-chain sugar nucleosides is described. The key intermediate in this synthesis, 3-deoxy-3-*C*-(2′-hydroxyethyl)-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**3**), was prepared by application of a Wittig reaction to 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuran-3-ulose (**1**). Compound **3** was hydrolyzed selectively to the 1,2-monoisopropylidene derivative **4**, which was converted *via* benzoylation and acetolysis into 1,2-diacetate **6**. Condensation of this compound with 6-benzamidochloromercuripurine in the presence of titanium tetrachloride, followed by deblocking with methanolic sodium methoxide, yielded the branched-chain nucleoside 9-[3-deoxy-3-*C*-(2′-hydroxyethyl)-β-D-allofuranosyl]adenine (**8**) in 48% yield based on **6**. In a separate procedure, 3-*C*-(carbomethoxymethyl)-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**2**) was degraded to 3-deoxy-3-*C*-(2′-hydroxyethyl)-1,2-*O*-isopropylidene-α-D-ribofuranose (**10**). The latter was then used in a parallel procedure to that used for the preparation of nucleoside **8** to prepare the branched-chain nucleoside 9-[3-deoxy-3-*C*-(2′-hydroxyethyl)-β-D-ribofuranosyl]adenine (**9**) in 37% yield based on the diacetate. The ORD and nmr spectra of the branched-chain sugar nucleosides are described.

In the preliminary communication,[1] we reported the synthesis of 3-deoxy-3-*C*-(2′-hydroxyethyl)-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**3**), the first branched-chain sugar of a series of branched-chain sugars prepared by application of the Wittig reaction to 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuran-3-ulose (**1**). We now wish to describe the synthesis of **3** in detail and in addition to describe its utilization in the preparation of two branched-chain sugar nucleosides **8** and **9**, each of which possesses a hydroxyethyl group in place of the secondary hydroxyl group on C-3 of the furanose ring.

Our interest in C-3′ branched-chain nucleosides stems partly from the fact that C-3′-modified nucleosides, for example, the antibiotic nucleoside cordycepin[2] and the

(1) This work was presented in part before the XXIst International Congress of Pure and Applied Chemistry, Prague, Czechoslovakia, Sept 1967, Abstracts, p N31, and in part before the Chemical Institute of Canada, Vancouver, Canada, June 1968, see *Chem. Can.*, **20**, 28 (1968); A. Rosenthal and L. (Benzing) Nguyen, *Tetrahedron Lett.*, 2393 (1967).

(2) J. J. Fox, K. A. Watanabe, and A. Bloch, *Progr. Nucleic Acid Res. Mol. Biol.* **5**, 251 (1966).