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Studies of Nucleosides and Nucleotides. LXXXV.[1] Purine Cyclonucleosides. (35). Synthesis of Purine Nucleosides having 2′-Azido and 2′-Amino Functions by Cleavage of Purine Cyclonucleosides

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8,2′-O-Cycloadenosine (I) was attacked by azide ion to give 8-oxy-2′-azide compound (II). The 8-oxy function of II was eliminated by derivatization to inosine (IV), acetylation to give V, chlorination with $POCl_3$ to VI, treatment with sodium methylmercaptide to give 6,8-bis(methylmercapto) compound (VII), reaction with dimethylamine to give VIII and Raney nickel dethiolation to give N^6-dimethyl-2′-amino-2′-deoxyadenosine (IX).

The compound VI was thiolated into X and treated with hydrogen peroxide to give 3′,5′-di-O-acetyl-2′-azido-2′-deoxyinosine (XI), which was deacetylated to 2′-azido-2′-deoxyinosine (XII). The compound XI was chlorinated and treated with ammonia to give 2′-azido-2′-deoxyadenosine.

Keywords——2′-deoxy-2′-azidoinosine; 2′-deoxy-2′-azidoadenosine; 2′-deoxy-2′-aminoadenosine; 2′-deoxy-2′-azido-N^6-dimethyladenosine; 2′-deoxy-2′-amino-N^6-dimethyladenosine; UV spectra; NMR spectra; paper chromatography; vilsmeier reagent

The use of cyclonucleosides has been shown to be a versatile method for introducing 2′-substituents into pyrimidine nucleosides.[3] In purine cyclonucleosides[4] it is necessary to eliminate the 8-oxy function after cleavage of cyclo bond. Since we have developed a method to convert 8-oxy-purine nucleosides to the ordinary nucleosides,[5] we attempted to synthesize 2′-azido and 2′-amino nucleosides by the cleavage of 8,2′-O-cyclonucleosides.

When 8,2′-anhydro-9-β-D-arabinofuranosyladenine[6] (8,2′-O-cycloadenosine, I) was heated with sodium azide in dimethylformamide (DMF) at 150°, a compound (II) having ultraviolet (UV) absorption similar to 8-oxyadenosine[7] was obtained in a yield of 80%. This compound showed a band at 2100 cm^{-1} in its infrared (IR) spectrum suggesting that an azido group was introduced. The structure of the 2′-azido-8-oxy compound (II) was further supported by its catalytic hydrogenation giving an amino nucleoside (III), which was revealed by ninhydrin as a violet spot on thin-layer chromatography (TLC). It also consumed periodate showing the presence of a cis aminoalcohol group.[8]

The compound (II) was then deaminated with barium nitrite in acetic acid to give a hypoxanthine derivative (IV), which migrated twice as fast as II in paper electrophoresis and showed a similar UV spectrum to that of 8-oxyinosine.[5] The compoound (IV) was

1) Part LXXIV of this series: M. Ikehara, T. Maruyama, and H. Miki, in preparation.
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3) *a*) D. Wagner, J.P.H. Verheyden, and J.G. Moffatt, *J. Org. Chem.*, **39**, 1654 (1974); *b*) K. Kikugawa, M. Ichino, T. Kusama, and T. Ukita, *Chem. Pharm. Bull.* (Tokyo), **17**, 798 (1969); *c*) R.P. Glinski, M.S. Khan, R.L. Kalamas, C.L. Stevens, and M.B. Sporn, *J. Org. Chem.*, **38**, 4299 (1973).
4) M. Ikehara, *Accounts of Chem. Res.*, **2**, 47 (1969) and subsequent papers.
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6) M. Ikehara and T. Maruyama, *Tetrahedron.*, **31**, 1369 (1975).
7) R.E. Holmes and R.K. Robins, *J. Amer. Chem Soc.*, **87**, 1772 (1965).
8) B. Lythgoe and A.R. Todd, *J. Chem. Soc.*, **1944**, 594; M. Viscontini, D. Hoch, and P. Karrer, *Helv. Chem. Acta.*, **38**, 642 (1955).

acetylated to give 3′,5′-di-O-acetyl-2′-deoxy-2′-azido-8-oxyinosine (V) in a yield of 60%. The compound (V) showed an IR band at 2100 cm^{-1}. The signals of H_2, and H_5, in the nuclear magnetic resonance (NMR) spectrum were shifted by the deshielding effect of the 2′-azido group.[3a)]

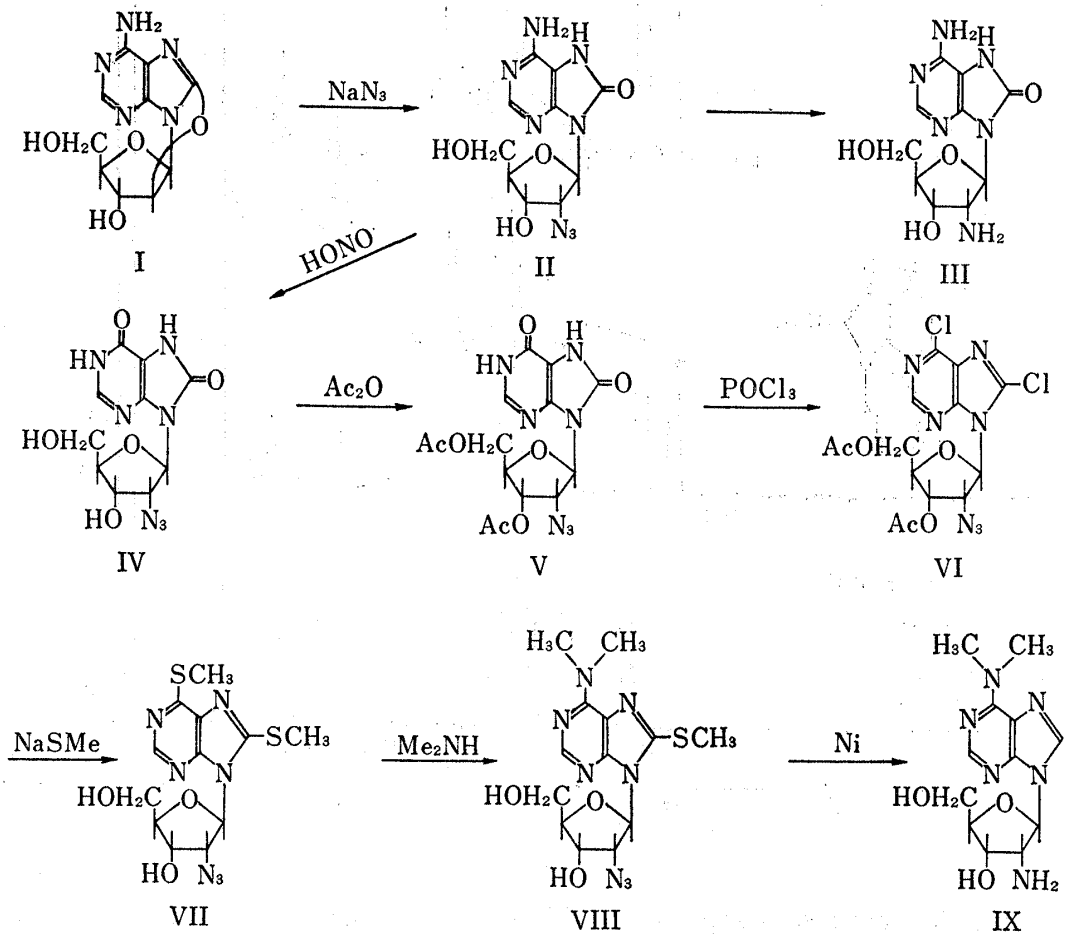

Chart 1

The compound (V) was then chlorinated using $POCl_3$ in tri-*n*-butylamine in conditions previously applied for the chlorination of 8-oxyinosine.[5)] After refluxing the mixture for 25 hrs, a compound (VI) having UV absorption similar to 6,8-dichloropurine riboside[9)] and IR band at 2100 cm^{-1} due to an azido group was obatined in a yield of 29%. In its NMR spectrum the signal of H_2, appeared at higher field than of H_3, showing that the N_3 group was intact.

2′-Azido-2′-deoxy-3′,5′-di-O-acetyl-6,8-dichloropurine riboside (VI) was allowed to react with $NaSCH_3$ in dioxane to give the 6,8-dimethylmercapto derivative (VII), as crystals of mp 183° in a yield of 52%. The position of the azido group was reconfirmed at this stage by NMR spectroscopy. As shown in Fig. 1, the signals of H-3′ and H-1′ were shifted significantly to the low field relative to that of ribosyl counterpart. Especially, the signal of 3′-OH proton shifted drastically due to a magnetic anisotropy of the 2′–azido group. The assignment of these signals have been done by the irradiation of H-5′ causing the decoupling of 5′-OH proton to a singlet and the irradiation of H-3′-causing the decoupling of 3′-OH as well as 4′-protons to a singlet and pseudo-triplet, respectively.

The compound (VII) was then heated with aqueous dimethylamine at 100° for 1 hr. 8-Methylmercapto-2′-azido-2′-deoxy-N^6-dimethyladenosine (VIII) was obtained in a yield

9) K.H. Boswell, L.F. Christensen, D.A. Shuman, and R.K. Robins, *J. Heterocycl. Chem.*, **12**, 1 (1975).

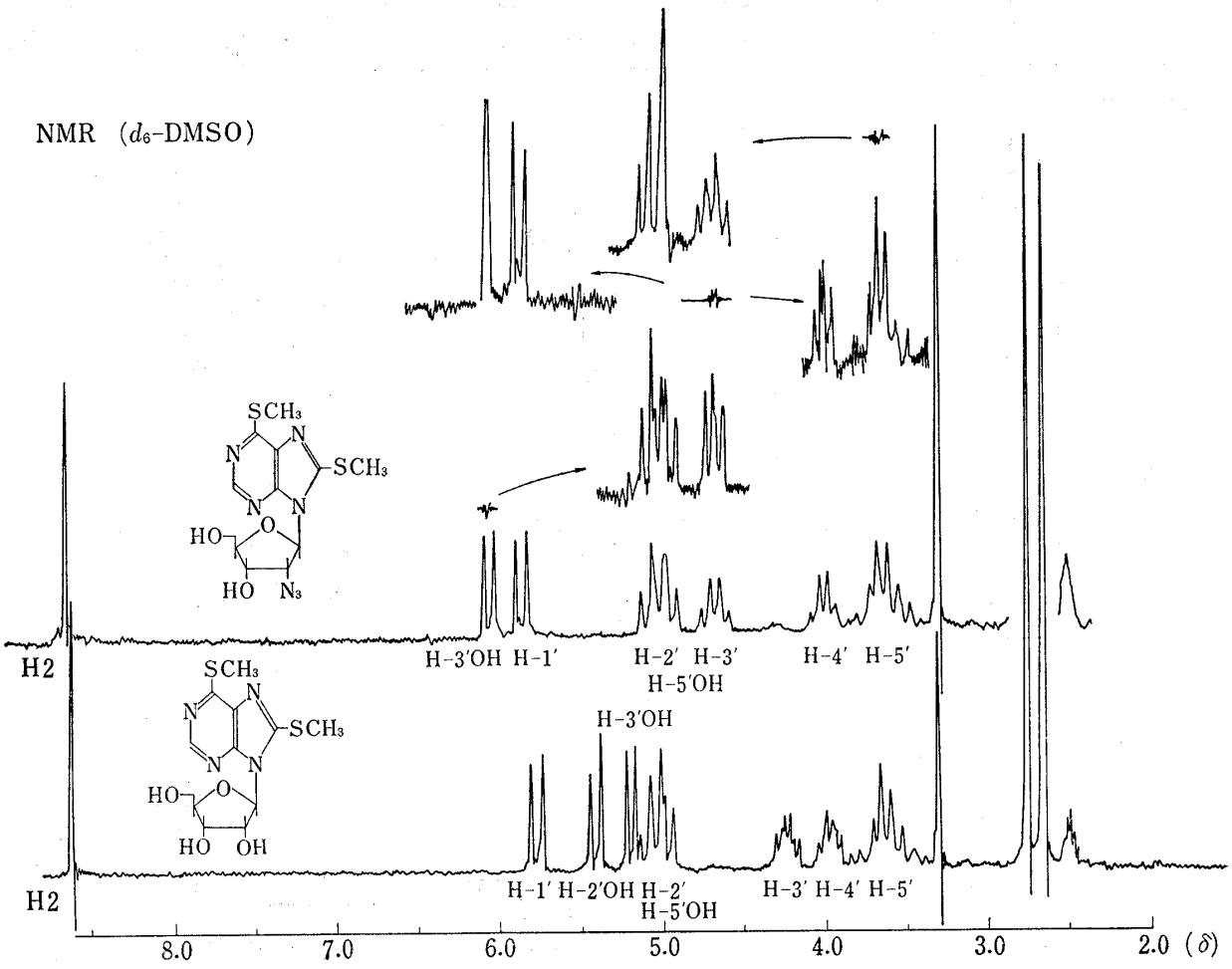

Fig. 1

of 44% as colorless needles of mp 151°. This compound showed an IR band of an azido group at 2100 cm^{-1} and a UV spectrum similar to 8-methylmercaptodimethyladenosine.[5] Elemental analysis also supported the structure of 8-methylmercapto-2'-azido-2'-deoxy-N-^{6} dimethyladenosine. Raney nickel reduction of the compound VIII gave 2'-amino-2'-deoxy-N^6-dimethyladenosine (IX), a positional isomer of puromycin aminonucleoside (3'-amino-3'-deoxy-N^6-dimethyldenosine).[10] Thus the introduction of azido and amino groups to the 2'-position starting from naturally occurring adenosine has been achieved.

In order to obtain a 2'-azido- and 2'-amno-2'-deoxyinosine or adenosine, the 2,6-dichloro-2'-azido compound (VI) was thiolated using thiourea in *n*-propanol. The structure of the resulting 6,8-dimercapto compound (X), mp 198°, was confirmed by IR and UV spectroscopy and derivatization to the 6,8-dimethylmercapto compound (VIII) by methylation with methyl iodide. When the 6,8-dimercaptopurine derivative (X) was treated with hydrogenperoxide in dioxane at 4° overnight as performed previously with 6,8-dimercaptopurine riboside,[5] a compound (XI) having a UV spectrum similar to inosine was obtained in a yield of 35%. The structure of XI was confirmed by deacetylation to give 2'-azido-2'-deoxyinosine (XII) which was identical with a sample obtained by the deamination of authentic 2'-azido-2'-deoxyadenosine.[11]

The compound XI was then chlorinated at the N^6-position by using $SOCl_2$-DMF in chloroform The resulting 6-chloro compound (XIII) was heated with methanolic ammonia

10) R.J. Suhadolnik, "Nucleoside Antibiotics," Wiley-Interscience, New York, 1970, p. 76.
11) M. Ikehara, T. Maruyama, and H. Miki, *Tetrahed. Letters*, **1976**, 4485.

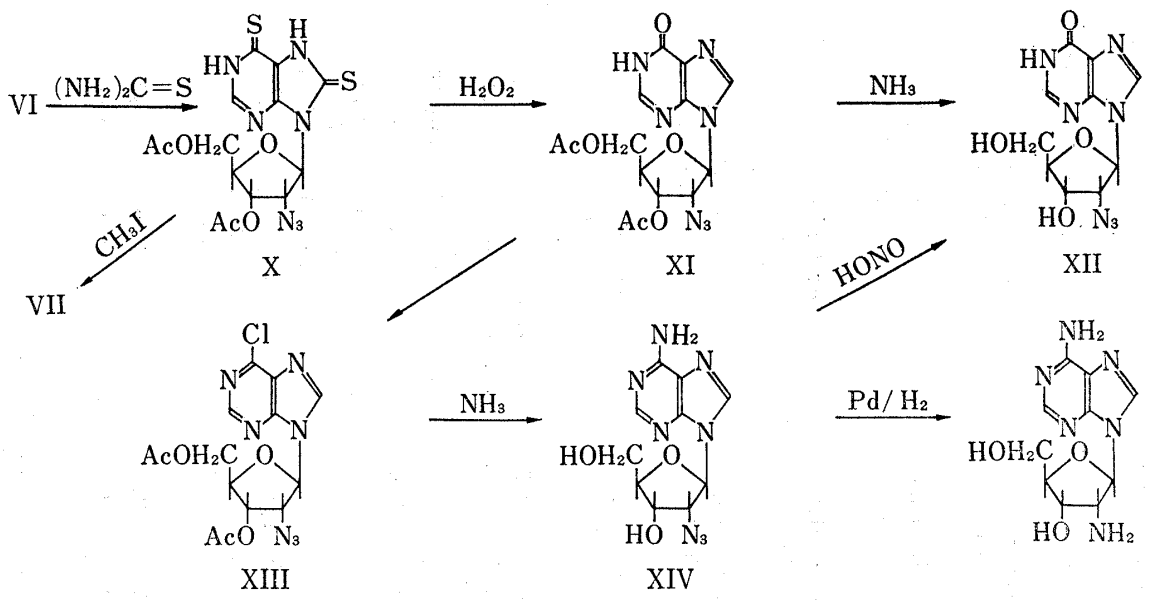

Chart 2

in a sealed tube to give 2′-azido-2′-deoxyadenosine (XIV) in an overall yield of 47%. This sample was identical to a sample obtained previously.[11] Since it has been shown that catalytic hydrogenolysis of compound (XIV) gave 2′-amino-2′-deoxyadenosine,[11,12] the present experiments establish a method for the introduction of 2′-azido and amino groups to purine nucleosides starting from naturally occurring adenosine.

Experimental

General Methods——UV absorption spectra were taken with a Hitachi EPS-3T spectrophotometer and IR spectra with a Hitachi EPI-G3 spectrophotometer. NMR spectra were taken with a Hitachi R-22 spectrometer operated at 90 MHz using dimethyl sulfoxide (DMSO)-d_6 as solvent and tetramethylsilane as internal standard.

TLC was performed on Kieselgel HF 254 plates using $CHCl_3$–EtOH as developing solvent. Column chromatography was perfomed on Mallinckrodt silica gel (100 mesh). Paper chromatography (PPC) was performed on Toyo filter paper No. 51A using the following solvent syatems: A, *n*-BuOH–H_2O (18: 46), B, iso-PrOH–conc. NH_4OH-H_2O (7: 1: 2), C, *n*-BuOH–AcOH–H_2O (5: 2: 3). Melting points were measured with a Yanagimoto hot stage and are uncorrected.

2′-Azido-2′-deoxy-8-oxyadenosine (II)——8,2′-O-cycloadenosine (5.04 g, 19 mmoles) was dissolved in anhydrous dimethyl formamide (DMF) (150 ml). Well-dried sodium azide (3.9 g, 14.7 mmoles) was added and the mixture was heated at 150° with stirring and exclusion of moisture. More sodium azide (3 g) was added after 2 hr and the heating was maintained for 1 hr. The colored reaction mixture was filtered and evaporated *in vacuo*. The residue was taken up in methanol (100 ml), insoluble material removed by centrifugation, and the solvent was evaporated. The residue was dissolved in *n*-butanol (250 ml) and washed with water (30 ml×2). Upon evaporation of butanol *in vacuo* the 2′-azido compound (II) was obtained as a hard syrup in a yield of 4.0 g (13.0 mmoles, 88%). UV: $\lambda_{max}^{H_2O}$ 268 nm, $\lambda_{max}^{pH\ 2}$ 262, 280 (sh); $\lambda_{max}^{pH\ 12}$ 279 nm. IR ν_{max}^{KBr} 2100 cm^{-1} (N_3). TLC: *Rf* 0.46 in $CHCl_3$–EtOH (3: 1).

2′-Amino-2′-deoxy-8-oxyadenosine (III)——The compound (II) (50 mg) was dissolved in ethanol–water (1: 1, 20 ml) and reduced under stirring with 20% palladium charcoal (50 mg) in a hydrogen atomosphere. After 30 min the catalyst was removed by filtration, and the filtrate was evaporated to a hard syrup. UV $\lambda_{max}^{H_2O}$ 267 nm; $\lambda_{max}^{pH\ 2}$ 261, 278 (sh); $\lambda_{max}^{pH\ 12}$ 278 nm. A band at 2100 cm^{-1} (N_3) in IR was not observed. Test by ninhydrin reagent showed a violet color suggesting the presence of an amino group. The periodate-benzidine test[11] showed *cis*-relationship for the OH and NH_2 groups.

3′-5′-Di-O-acetyl-2′-azido-2′-deoxy-8-oxyinosine (V)——The compound (III) (3.33 g, 10.8 mmoles) was dissolved in acetic acid (6 ml) and water (94 ml). Barium nitrite (5.61 g, 22.6 mmoles) was added and the mixture was kept at room temperature overnight. Barium ions were precipitated by the addition of $(NH_4)_2$-SO_4 (45.4 ml) and the precipitate was removed by centrifugation. Supernatant and washings were combined

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TABLE I. NMR Spectral Properties of 2′-Azido Nucleosides and Reference Compounds

	H-2		H-1′	H-2′	H-3′	H-4′	H-5′	2′-OH	3′-OH	5′-OH
8-OH-tri-Ac-inosine (δ) (A)	8.18 s, 1	N1-H, N7-H 12.50, br, 1 11.25, br, 1	6.00—6.35 m, 2		5.74 t, 1 $J_{2'3'}=5$	4.10—4.70 m, 3			Ac 2.13 s, 6 2.18 s, 3	
8-OH-2′-N_3-diAc-inosine (V) (A)	8.10 s, 1		5.96 d, 1 $J_{1'2'}=6$	5.33 t, 1 $J_{2'3'}=6$	5.70 m, 1	4.20—4.60 m, 3			Ac 2.21 s, 3 2.07 s, 3	
6,8-diCl-purine riboside (A)	8.76 s, 1		6.25 m, 2		5.83 t, 1 $J_{2'3'}=J_{3'4'}=5$	4.20—4.60 m, 3			Ac 2.17 s, 3 2.09 s, 3 2.01 s, 3	
6,8,-diCl-2′-N_3-2′-deoxy purine riboside(VI) (A)	8.78 s, 1		6.03 d, 1 $J_{1'2'}=6$	5.63 t, 1 $J_{2'3'}=6$	5.86 q, 1 $J_{3'4'}=3$	4.10—4.60 m, 3			Ac 2.27 s, 3 2.05 s, 3	
8-OH-tri-Ac-diMe-adenosine (A)	8.21 s, 1	$(CH_3)_2N$- 3.29 s, 6	6.16 m, 2		5.75 m, 1	4.10—4.50 m, 3			Ac 2.11 s, 3 2.09 s, s, 3 2.04 s, 3	
6,8-di-SCH_3-purine riboside (B)	8.63 s, 1	SMe 2.78 s, 3 2.68 s, 3	5.78 d, 1 $J_{1'2'}=6$	5.02 m, 1 $J_{2'3'}=6$	4.23 hexa, 1 $J_{3'4'}=6$	3.98 hexa, 1 $J_{4'5'}=5$	3.63 m, 1	5.41 d, 1 $J_{2'2'}$ -OH=5	5.22 d, 1 $J_{3'3'}$ -OH=5	5.03 t, 1 $J_{5'5'}$ -OH=6
6,8-di-SMe-2′-N_3-2′-deoxypurine riboside (VII) (B)	8.67 s, 1	SMe 2.78 s, 3 2.67 s, 3	5.89 d, 1 $J_{1'2'}=6$	5.10 t, 1 $J_{2'3'}=6$	4.68 q, 1 $J_{3'4'}=5$	4.03 q, 1 $J_{4'5'}=5$	3.67 m, 2		6.09 d, 1 $J_{3'3'}$ -OH=6	4.98 t, 1 $J_{5'5'}$ -OH=6u
8-SMe-triAcdiMe-adenosine (A)	8.23 s, 1	$(Me)_2N$ 3.18 s, 6 SMe 2.71 s, 3	6.10 p, 1 $J_{1'2'}=5$	6.28 q, 1 $J_{2'3'}=6$	5.84 t, 1 $J_{3'4'}=6$	4.20—4.70 m, 3			Ac 2.13 s, 3 2.07 s, 3 2.04 s, 3	
8-SMe-2′-N_3-diMe-adenosine (VIII) (C)	8.13 s, 1	$(Me)_2N$ 3.53 s, 6 SMe 2.77 s, 3	6.03 d, 1 $J_{1'2'}=8$	4.88 q, 1 $J_{2'3'}=5$	4.72 m, 1 $J_{3'4'}=4$	4.27 q, 1 $J_{4'5'}=2$	3.80 m, 2		6.05 br, 1	5.13 m, 1

solvent A; $CDCl_3$ B; d_6-DMSO C; d_6-acetone

and evaporated *in vacuo*. The residue was dissolved in ethanol (100 ml) and insoluble material was filtered off. The solvent was evaporated and 2′-azido-2′-deoxy-8-oxyinosine (IV) was obtained as a hygroscopic caramel in a yield of 2.387 g (7.8 mmoles, 72%). UV $\lambda_{max}^{H_2O}$ 257, 280 nm (sh); $\lambda_{max}^{pH\,2}$ 257, 280 (sh); $\lambda_{max}^{pH\,12}$ 273.

This material was dissolved in pyridine (100 ml) and concentrated to about 70 ml. To the solution, acetic anhydride (30 ml) was added and the mixture was stirred at room temperature for 1 hr. The solvent was evaporated *in vacuo*, and traces of pyridine were removed completely by coevaporation several times with toluene. The residue was dissolved in *n*-butanol (100 ml), washed with water (20 ml × 2) and evaporated to give a hard syrup (2.47 g, 6.2 mmoles, 56%). UV: $\lambda_{max}^{50\%EtOH}$ 256, 280 nm (sh); $\lambda_{max}^{pH\,2}$ 256, 280 (sh); $\lambda_{max}^{pH\,12}$ 271. IR: $\nu_{max}^{CHCl_3}$ 2100 cm^{-1} (N_3). NMR data are summarized in Table I. TLC: *Rf* 0.53 in $CHCl_3$–EtOH (8: 1).

When the deamination was performed with sodium nitrite in acetic acid, the compound V was obtained in a yield of 48%.

6,8-Dichloro-9-β-(3′,5′-di-O-acetyl-2′-azido-2′-deoxy-D-ribofuranosyl)purine (VI)——The compound (V) (1.12 g, 28 mmoles) was dissolved in phosphorus oxychloride (18 ml) and tri-*n*-butylamine (1.8 ml, dried by azeotropic evaporation with benzene). The mixture was refluxed for 7.5 hr. During that time tri-*n*-butylamine (0.8 ml) was added every 2 hr. Analysis of the reaction extent by TLC ($CHCl_3$–EtOH, 15: 1) showed spots at *Rf* 0.85 (dichlorinated compound), *Rf* 0.50 (monochlorinated compoud) and *Rf* 0.22 (starting material). The ratio of di- to monochloro compound being 11: 2. Phosphorus oxychloride was evaporated *in vacuo*, the residue was poured into ice, and the product was extracted with $CHCl_3$. The $CHCl_3$–layer was washed with water, dried over $MgSO_4$ and evaporated. The residue was dissolved in a small amount of $CHCl_3$ and applied to a column (3.6 × 7.2 cm) of silica gel. Elution with 3% EtOH–$CHCl_3$ (500 ml) and 10% EtOH–$CHCl_3$ (100 ml) gave a mixture of mono- and dichlorinated compounds. They were again applied to a column (2.3 × 34.3 cm) of silica gel and eluted with 1% EtOH–$CHCl_3$. Evaporation of the solvent gave the compound (VI) in a yield of 0.4 g (0.8 mmole, 29%). UV $\lambda_{max}^{50\%EtOH}$ 251, 268, 280 (sh) nm; $\lambda_{max}^{pH\,2}$ 251, 268, 280 (sh), $\lambda_{max}^{pH\,12}$ 250, 270. IR: $\nu_{max}^{CHCl_3}$ 2100 cm^{-1} (N_3). NMR data are summarized in Table I. TLC *Rf* 0.71 in $CHCl_3$–EtOH (10: 1).

6,8-Bis(methylmercapto)-9-β-(2′-azido-2′-deoxy-D-ribofuranosyl)purine (VII)——i) The dichloro compound (III) (200 mg, 0.46 mmole) was dissolved in dioxane (20 ml), 20% sodium methylmercaptide (2.8 ml) was added, and the mixture was stirred for 18 hr at room temperature. The water-layer was removed by suction with a pipette and the dioxane solution was neutralized with 2N HCl. The solvent was evaporated with a trap of 5N NaOH for trapping methyl-mercaptan. To the residue a small amount of water was added and isoluble material was collected by filtration. This material was recrystallized from EtOH to give pale yellow needles, mp 181—183°, in a yield of 90 mg, (0.24 mmole, 52%). *Anal.* Calcd. for $C_{12}H_{15}O_3N_7S_2$: C, 39.16; H, 4.09; N, 26.54; S, 17.40. Found: C, 39.19; H, 4.35; N, 26.02; S, 17.12. UV data are collected in Table II. NMR data are collected in Table I and Fig. 1. IR: ν_{max}^{KBr} 2095, 2115 cm^{-1} (N_3). TLC: *Rf* 0.45 in $CHCl_3$–EtOH (10: 1).

Table II. UV Absorption Propeerties of Azido Nucleosides and Reference Compounds

UV λ_{max} nm (ε)	Neutral[a]	pH 2	pH 12
8-OH-TriAc-inosione	256.5 (12300) 280 (6500)	256.5 (12300) 280 (6500)	273.5 (15300)
8-OH-Tri-Ac-diMeadenosine	282 (15300)	277 (13800)	295 (18900)
6,8-di-SMe-adenosine	248 (13800) 311 (23000) 305 (sh, 22200)	248.5 (15500) 312 (20000) 305 (sh, 18800)	248 (16800) 311.5 (23000) 305 (sh, 22300)
6,8-Di-SMe-2′-N3-purine riboside (VII)	247 (18100) 310 (23700) 303 (sh, 22700)	247 (18100) 310 (23700) 303 (sh, 22700)	247 (18100) 310 (23500) 303 (sh, 22400)
8-SMe-triAc-diMeadenosine (VIII)	292 (19500) 231 (17200)	290 (19400)	294 (20500)
8-SMe-2′-N3-diMeadenosine (IX)	291.5 (18800) 230 (16800)	289 (19400) 215 (sh, 17900)	292 (18800)

a) solvent 50% EtOH

ii) The 6,8-dimercapto compound (X) (10 mg) was dissolved in EtOH (3 ml) and H_2O (1 ml). 1N NaOH (0.5 ml) and methyl iodide (0.1 ml) were added and the mixture was stirred at room temperature overnight. After neutralization with 1N HCl, the mixture was evaporated and separated by preparative TLC ($CHCl_3$–EtOH 10: 1). A substance migrating in a band at *Rf* 0.45 was collected. Recrystallization from EtOH gave crystals of mp 185°. This sample was identical with that obtained in i). UV: $\lambda_{max}^{50\%EtOH}$ 245, 302, 310 nm.

8-Methylmercapto-2′-azido-2′-deoxy-N⁶-dimethyladenosine (VIII)——The bis(methylmercapto) compound (VII) (30 mg, 0.08 mmoles) was dissolved in 40% dimethylamine (3 ml) and heated at 100° for 12 hr

in a sealed tube. The mixture was applied to a preparative TLC on silica gel. Material migrating at *Rf* 0.33 was collected by filling into a column and elution with $CHCl_3$–EtOH (9: 1). Evaporation of the solvent gave a residue, which was recrystallized from EtOH to give white needles, mp 150—151° in a yield of 13 mg (0.035 mmole, 44%). *Anal.* Calcd. for $C_{13}H_{18}O_3N_8S$: C, 42.45; H, 5.02; N, 30.36. Found: C, 42.62; H, 4.95; N, 30.58. UV data are collected in Table II. NMR are on Table I. TLC: *Rf* 0.40 in $CHCl_3$–EtOH (10: 1).

2′-Amino-2′-deoxy-N⁶-dimethyladenosine (IX)——The compound (VIII) (20 mg) was dissolved in EtOH (8 ml) and H_2O (1 ml). Raney nickel (*ca.* 0.1 ml) was added and the mixture was refluxed for 1 hr with stirring. Raney nickel was filtered off and the filtrate was evaporated *in vacuo* to afford a glass. UV $\lambda_{max}^{H_2O}$ 275 nm, $\lambda_{max}^{pH\ 2}$ 268, $\lambda_{max}^{pH\ 12}$ 274. PPC: *Rf* (B) 0.73, *Rf* (C) 0.65. TLC: *Rf* 0.16 in $CHCl_3$–EtOH (3: 1). These spots were revealed by their violet color with ninhydrin spray. Cochromatography with 3′-amino-3′-deoxy-N⁶-dimethyladenosine derived from puromycin[12] showed that these two compounds have the same *Rf* value in PPC.

6,8-Dimercapto-9-β-(3′-5′-di-O-acetyl-2′-azido-2′-deoxy-D-ribofuranosyl)purine (X)——The 6,8-dichloro-2′-azido compound (VI) (496 mg, 1.15 mmoles) was dissolved in isopropanol (15 ml) and refluxed with thiourea (880 mg, 11.6 mmoles) for 15 min. The solvent was evaporated and the residue was taken up with ethyl acetate. The ethyl acetate solution was washed twice with water, dried over $MgSO_4$, and evaporated *in vacuo*. Concentration of ethyl acetate gave pale yellow crystals, mp 194—198°, in a yield of 160 mg. (0.38 mmoles, 33%). From the mother liquor a further 110 mg of the product was obtained. UV: $\lambda_{max}^{50\%EtOH}$ 268, 358 nm, $\lambda_{max}^{pH\ 2}$ 268, 358; $\lambda_{max}^{pH\ 12}$ 262, 335. IR: ν_{max}^{KBr} 2100 cm^{-1} (N_3). TLC: *Rf* 0.39 in $CHCl_3$–EtOH (20: 1).

3′,5′-Di-O-acetyl-2′-azido-2′-deoxyinosine (XI)——i) The 6,8-dimercapto compound X (110 mg, 0.26 mmole) was dissolved in dioxane (5.5 ml) and 30% aq H_2O_2 (1.4 ml) was added. After keeping the mixture at 4° overnight, unreacted H_2O_2 was decomposed with MnO_2. The mixture was filtered and filtrate was evaporated. The residue was dissolved in $CHCl_3$ and applied to preparative TLC ($CHCl_3$–EtOH, 7: 1). A band migrating at *Rf* 0.42 was collected. The diacetyl-2′-azido compound (XI) was obtained as a glass in a yield of 34 mg (0.09 mmole, 35%). *Anal.* Calcd. for $C_{14}H_{15}O_6N_7$: C, 44.56; H, 4.01; N, 25.99. Found: C, 44.67; H, 3.77; N, 26.00. UV: $\lambda_{max}^{50\%EtOH}$ 248 nm, $\lambda_{max}^{pH\ 2}$ 248, $\lambda_{max}^{pH\ 12}$ 254. IR: ν_{max}^{KBr} 2125 cm^{-1} (N_3).

ii) 2′-Azido-2′-deoxyadenosine[10] XIV (95 mg, 0.33 mmole) was dissolved in 50% AcOH (10 ml) and sodium nitrite (95 mg) was added. The mixture was kept at room temperature overnight. More sodium nitrite (100 mg) was added and the mixture was kept for further 12 hr. The solvent was evaporated and the residue was dissolved in pyridine (2 ml). To the solution acetic anhydride (0.5 ml) was added. After keeping the mixture overnight, the solvent was evaporated. Recrystallization from EtOH gave 42 mg (0.11 mmole, 33%) of diacetyl-2′-azidoinosine, mp 182—183°. This sample was identical with that obtained in i).

2′-Azido-2′-deoxyinosine (XII)——Diacetyl-2′-azido-2′-deoxyinosine XI (20 mg) was dissolved in methanolic ammonia (saturated at 0°, 3 ml). The tightly stoppered flask was kept at room temperature overnight. The mixture was evaporated and the residue was recrystallized from EtOH. PPC: *Rf* (A) 0.35 *Rf* (B) 0.64, *Rf* (C) 0.58. UV: $\lambda_{max}^{H_2O}$ 250 nm, $\lambda_{max}^{pH\ 2}$ 248, $\lambda_{max}^{pH\ 12}$ 253. NMR: δ 8.39 (s, 1H, H-8), 8.07 (s, 1H, H-2), 6.03 (d, 1H, H-1, $J_{1'-2'}=6$ Hz), 5.02 (t, 1H, H-2′, $J_{2'-3'}=5$ Hz), 5.60 (m, 1H, 3′-H), 4.43 (m, 3H, 4′ and 5′-H).

2′-Deoxy-2′-azidoadenosine (XIV)——3′,5′-Diacetyl-2′-azido-2′-deoxyinosine XI (50 mg) was dissolved in $CHCl_3$ (20 ml) containing $SOCl_2$ (180 mg) and DMF (30 mg). After refluxing for 3 hr with exclusion of moisture the reaction mixture was kept at room temperature overnight. The solvent was evaporated with exclusion of moisture and the residual syrup was dissolved in methanolic ammonia (saturated at 0°, 10 ml). The mixture was heated ar 140—150° for 8 hr in a sealed tube. After careful evaporation of the solvent the residue was dissolved in $CHCl_3$. The solution was washed twice with H_2O and $CHCl_3$ was evaporated *in vacuo*. 2′-Azido-2′-deoxyadenosine, mp 214—216°, was obtained in a yield of 18 mg (46%). *Anal.* Calcd. for $C_{10}H_{12}O_3N_8$: C, 41.09; H, 4.14; N, 38.34. Found: C, 41.37; H, 3.87, N, 38.04. UV: $\lambda_{max}^{H_2O}$ 257 nm, $\lambda_{max}^{pH\ 2}$ 257, $\lambda_{max}^{pH\ 12}$ 259. IR: ν_{max}^{KBr} 2110, 2130 cm^{-1} (N_3). PPC: *Rf* (A) 0.20, *Rf* (B) 0.40, *Rf* (C) 0.40. These properties were completely identical with an authentic sample.[12]