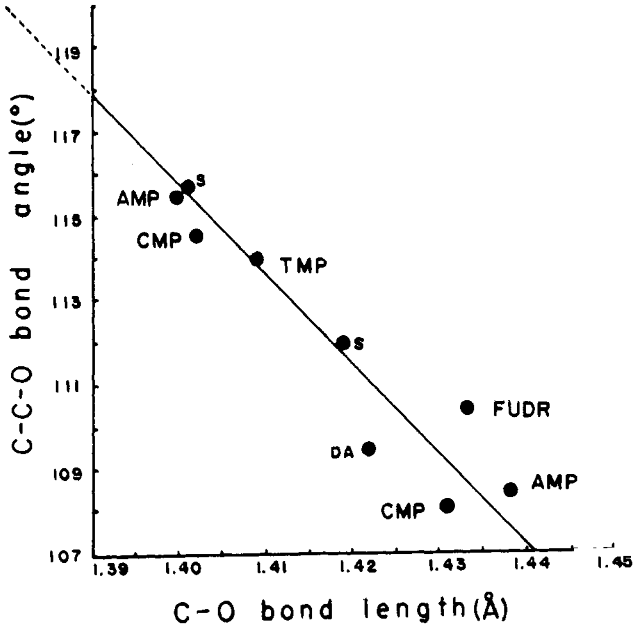

Figure 8. Graph of C–O bond lengths *vs.* C–C–O external bond angle. S is the abbreviation for sucrose.

in the fructofuranosyl moiety are displaced quite appreciably and by about the same amount from the plane of the other three atoms (Table V), in contrast to the other examples cited, where the displacement of one of the atoms is more pronounced than the other.

The dependence of the C–O bond length on the C–C–O external bond angle may be represented by the straight-line graph as illustrated in Figure 8. All the points in the graph were given equal weight. The slope of the line indicates that for every degree increase in the C–C–O external bond angle the C–O distance shortens by about 0.0047 Å. Theoretically, therefore, for external angles of 120 and 129.5° the extrapolated C–O bond lengths will be 1.380 and 1.347 Å., respectively. The latter is the case when the carbon atom attached to the oxygen atom lies in the plane of the adjacent carbon atoms in the ring. These values may be compared with the values for the C–O distances in carbonyl and carboxylate groups. Interestingly, the C–O bond shortens only when it is in the equatorial orientation, while the axial C–O bond (in DA) possesses a normal value. The rehybridization of the carbon atom apparently results in a gain in the sp^2 character of the C–O bond (equatorial) and a gain in the p-character of the C–H bond (axial). These ideas may find possible application in assigning conformations to furanosides from p.m.r. studies.

Acknowledgment. The author gratefully thanks Professor L. H. Jensen and Dr. D. G. Watson of this department and Dr. W. S. Chilton of the Department of Chemistry for their interest and helpful criticism of the manuscript, and Drs. G. M. Brown, H. A. Levy, D. G. Watson, D. J. Sutor, and P. Tollin for access to data in advance of publication.

Studies of Nucleosides and Nucleotides. XXIV.[1] Purine Cyclonucleosides. I. 8,2′-Cyclonucleoside Derived from 2-Chloro-8-mercapto-9-β-D-xylofuranosyladenine[2]

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The synthesis of 2-chloro-8-mercapto-9-(2′-O-acetyl-3′-O-tosyl-5′-O-methoxycarbonyl-β-D-xylosyl)adenine (IV) was achieved by Davoll's method. Compound IV gave 8,2′-anhydro-2-chloro-8-mercapto-β-D-arabinofuranosyladenine (V) on treatment with sodium methoxide in methanol. The structure of V was elucidated by chemical and physical methods. Desulfurization of V with Raney nickel followed by hydrogenation over palladized charcoal gave 2′-deoxyadenosine, identical with naturally occurring nucleoside. Hydrolysis of V in acidic and alkaline media was investigated.

Among the various reactions of nucleosides, increasing interest is being shown in the synthesis of cyclonucleosides[3] (anhydronucleosides) because of their utility in the elucidation of anomeric configurations[4] and in serving as precursors for chemical alteration of the sugar moiety.[5] Previous studies in this area have been restricted mainly to pyrimidine nucleosides.[6]

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(1) Part XXIII of this series: M. Ikehara, F. Ishikawa, and H. Uno, *Chem. Pharm. Bull.* (Tokyo), **12**, 267 (1964).

(2) The preliminary account of this work has been reported: M. Ikehara and H. Tada, *J. Am. Chem. Soc.*, **85**, 2344 (1963).

(3) J. J. Fox and I. Wempen, *Advan. Carbohydrate Chem.*, **14**, 283 (1959).

(4) V. M. Clark, A. R. Todd, and J. Zussman, *J. Chem. Soc.*, 2959 (1951); W. Anderson, D. H. Hayes, A. M. Michelson, and A. R. Todd, *ibid.*, 1882 (1954); B. R. Baker and J. P. Joseph, *J. Am. Chem. Soc.*, **77**, 15 (1955); R. W. Chambers, J. G. Moffatt, and H. G. Khorana, *ibid.*, **79**, 3747 (1957).

(5) D. M. Brown, A. R. Todd, and S. Varadarajan, *J. Chem. Soc.*, 2388 (1950); A. M. Michelson and A. R. Todd, *ibid.*, 816 (1955); J. J. Fox and N. C. Miller, *J. Org. Chem.*, **28**, 936 (1963), and previous papers by J. J. Fox and collaborators; J. H. Horwitz, J. Chua, J. A. Urbansky, and M. Noel, *ibid.*, **28**, 942 (1963).

(6) During the course of this investigation, a study by Holmes and Robins[7] dealing with the synthesis of a 3,5′-cyclonucleoside from a cyclonucleoside salt[8] of a purine nucleoside appeared.

(7) R. E. Holmes and R. K. Robins, *J. Org. Chem.*, **28**, 3483 (1963).

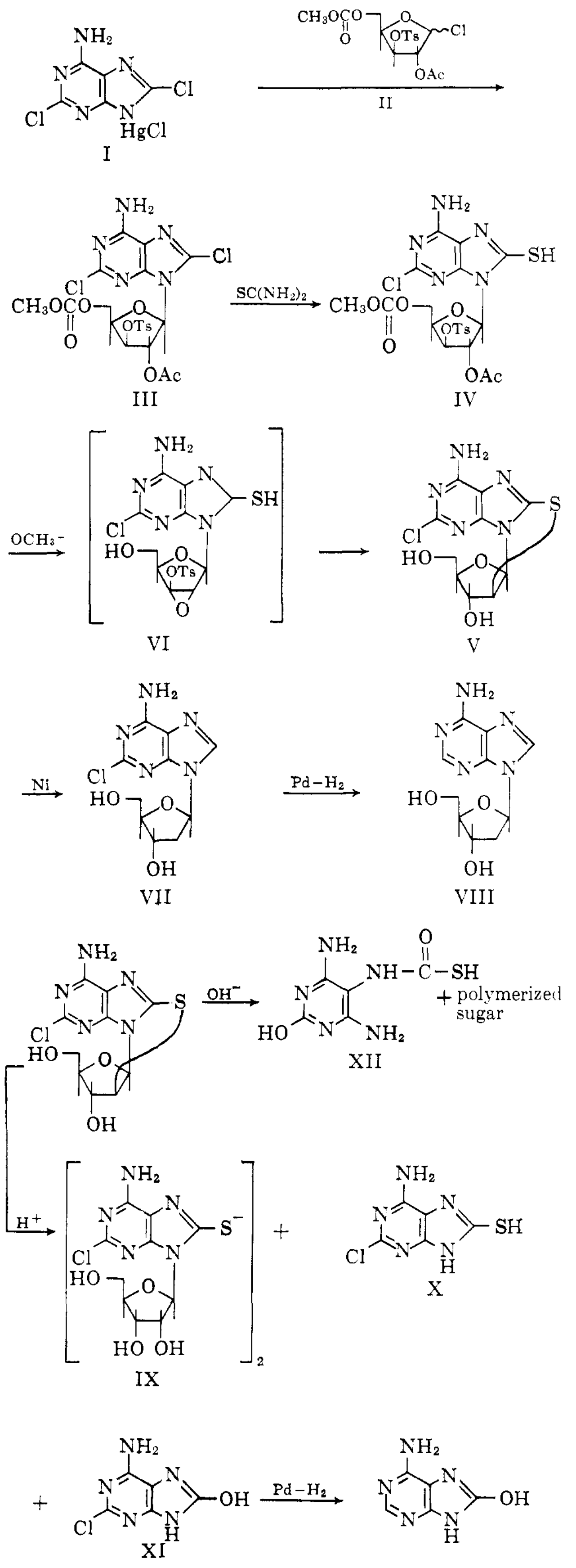
(8) See V. M. Clark, *et al.*, ref. 4.

As a part of our program[9] on the interaction of several enzymatic systems with nucleotides, we undertook the synthesis of a cyclonucleoside in the purine series. X-Ray crystallographic analysis has shown[10] that a structural analogy exists between the 2-carbonyl (or 2-thione) of a pyrimidine nucleoside and the 8-hydroxy (or 8-mercapto) group of 8-hydroxy or 8-mercaptopurine nucleosides in relation to the sugar moiety.[11]

A suitable intermediate for the formation of an 8,2′-anhydropurine nucleoside would be a 2′,3′-epoxyribofuranosyl derivative of an 8-mercaptopurine.[12]

By analogy with the work of Reist, *et al.*,[13] the 2′,3′-anhydroribofuranosyl sugar would be expected to be cleaved by the rearward attack of the 8-mercapto group on C-2′ or C-3′. 2,8-Dichloroadenine chloromercury salt (I) was condensed (see Chart I) with 2-*O*-acetyl-3-*O*-tosyl-5-*O*-methoxycarbonyl-D-xylofuranosyl-chloride[14] (II) in refluxing xylene to give III in 27% yield. In order to limit the introduction of a mercapto group to 8-position only, compound III was allowed to react in *n*-butyl alcohol with thiourea at reflux temperature for 8 hr. 2-Chloro-8-mercapto-9-(2′-*O*-acetyl-3′-*O*-tosyl-5′-*O*-methoxycarbonyl-D-xylofuranosyl)adenine (IV) was obtained as a hard glass in 92% yield. The characterization of IV as an 8-mercapto derivative is indicated by its intense ultraviolet absorption band at 300 mμ. Considering the higher reactivity of the 8- *vs.* the 2-chloro atom[15] and the further transformation of IV to the 8,2′-cyclo derivative,[16] it must be concluded that substitution of the 2-chloro atom did not occur. Compound IV was then refluxed briefly with 3 moles of sodium methoxide in anhydrous methanol. After removal of sodium ion with ion-exchange resin and evaporation of solvent a crystalline substance, m.p. 228–229°, was obtained in 41% yield. The ultraviolet absorption spectrum of this material showed a maximum at 280 mμ in both acidic and alkaline media, which indicated the conversion of mercapto group to a nondissociable sulfur. Elemental analytical data was consistent with the structure of 8,2′-anhydro-2-chloro-8-mercapto-9-β-D-arabinofuranosyladenine (V). Another possible structure could be VI, 2-chloro-8-mercapto-9-(2′,3′-anhydro)-β-D-ribofuranosyladenine. However VI is excluded by the fact that the infrared absorption spectrum of compound V showed no band at 863 cm.$^{-1}$ (assigned to the epoxide group by Anderson, *et al.*[14]). Further support of structure V was obtained by nuclear magnetic resonance (n.m.r.) spectrum. Compound V showed a doublet signal around 405 c.p.s., which was assigned to the H-1′ proton.[17] The spin–spin coupling of this band caused

Chart I



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(9) M. Ikehara, E. Ohtsuka, S. Kitagawa, K. Yagi, and Y. Tonomura, *J. Am. Chem. Soc.*, **83**, 2679 (1961); N. Azuma, M. Ikehara, E. Ohtsuka, and Y. Tonomura, *Biochim. Biophys. Acta*, **60**, 104 (1962); M. Ikehara, E. Ohtsuka, S. Kitagawa, and Y. Tonomura, *ibid.*, **82**, 74 (1964).

(10) M. Wilkins, "Nucleoproteins," R. Stoops, Ed., Interscience Publishers, Inc., New York., N. Y., 1959, p. 48.

(11) This relationship was observed on Stuart or Dreiding molecular models.

(12) Direct condensation of hydroxypurine chloromercury salt with acetylated halogenosugar gave a colored resinous material and seems to be unsuitable for the present purpose (unpublished experiment by H. Tada).

(13) E. J. Reist, J. H. Osiecki, L. Goodman, and B. R. Baker, *J. Am. Chem. Soc.*, **83**, 2208 (1961).

(14) C. D. Anderson, L. Goodman, and B. R. Baker, *ibid.*, **81**, 3967 (1959).

(15) E. Y. Sutcliffe and R. K. Robins, *J. Org. Chem.*, **28**, 1662 (1963).

(16) The formation of an anhydro linkage between positions 2 and 2′ or 3′ may be excluded by the relatively long distance between these atoms as observed on molecular models.

(17) W. W. Lee, A. Benitez, C. D. Anderson, L. Goodman, and B. R. Baker, *J. Am. Chem. Soc.*, **83**, 1906 (1961).

Table I. Comparison of Properties of Synthetic and Natural 2′-Deoxyadenosine

	Synthetic (VIII)	Natural	Reported[a]
M.p., °C.	185–189[b]	186–189[b]	186–189
M.m.p., °C.	186–188[b]		
[α] D, deg.	−25.8 (c 0.75, H_2O)	−26.1[c] (c 1.0, H_2O)	−26 ± 3[d] (c 1.0, H_2O)
$\lambda_{max}^{0.1N HCl}$, mμ	258	258	258
$\lambda_{max}^{0.1N NaOH}$, mμ	260	260	260
R_f (H_2O, pH 10.0)	0.50	0.50	0.50
N.m.r.[e], c.p.s.	404 (triplet)	404 (triplet)	405[f] (triplet)

[a] Ref. 14. [b] Uncorrected. [c] Temp., 20°. [d] Temp., 23°. [e] Signal of C-1′ proton, taken in pyridine. [f] Taken in D_2O.

by the H-2′ proton was 7 c.p.s. (adenosine gives 5 c.p.s.).[18] This value indicates that the configuration in V of H-1–H-2′ is *cis*. Furthermore, the H-1′ signal appeared in lower magnetic field relative to the signal of the H-1′ of 2′-deoxyadenosine. This fact may be explained by substitution with SR (8,2′-anhydro linkage) at C-2′.[19,20]

The position of the anhydro linkage of V was further confirmed by transformation of this compound to 2′-deoxyadenosine. Compound V was refluxed in 50% ethanol with Raney nickel for 1.5 hr. The resulting glass (VII) showed an ultraviolet absorption maximum at 265 mμ which was similar with that of 2-chloroadenosine[22] and 2-chloro-2′-deoxyadenosine.[23] Paper chromatographic examination (in water, pH 10) of VII and the color test[24] of the acidic hydrolysate of VII indicated that VII is 2-chloro-2′-deoxyadenosine. The glass (VII) was hydrogenated over palladized charcoal. Crystalline VIII was obtained and compared directly with an authentic sample[25] of natural 2′-deoxyadenosine by mixture melting point, color reaction,[26,27] optical properties, and paper chromatography (see Table I). The sample VII was shown to be definitely different from synthetic 3′-deoxyadenosine.[2,14]

From these experimental results, it is concluded that the anhydro linkage of compound V is between the 8- and 2′-position and not between the 8- and 3′-position. The ease of attack of the 8-mercapto group on the 2′- rather than on the 3′-carbon may be explained by the configurational proximity of the 8- and 2′-position as in the case of pyrimidine nucleosides.[28] Thus the 8,2′-anhydro method established a new and simple pathway leading to the synthesis of 2′-deoxynucleosides in the purine series.

The hydrolytic cleavage of the 8,2′-anhydro linkage of compound V was then investigated. In contrast to our expectation, compound V was resistant to treatment with refluxing 0.1–0.5 *N* hydrochloric acid or sodium hydroxide solution. This stability may be ascribed to the unstrained five-membered thiazolidine ring.[29] However, more drastic hydrolytic conditions caused cleavage of 8,2′-anhydro bond. When compound V was refluxed in 2 *N* sulfuric acid for 100 min., several ultraviolet-absorbing spots were observed by paper chromatography. Examination of the products separated by preparative paper chromatography showed the presence of 2-chloro-9-β-D-ribofuranosyladenine-(8) disulfide (IX), 2-chloro-8-hydroxyadenine (X), 2-chloro-8-mercaptoadenine (XI), and a substance having unknown structure.[31]

The structure of compounds X and XI was elucidated by ultraviolet absorption, paper chromatography, and comparison with the authentic specimen. The disulfide structure of IX was deduced from optical and paper chromatographic behavior as observed earlier in the case of 8-mercaptoguanosine.[32] Reduction of IX with Raney nickel gave 2-chloroadenine 9-glycoside, and the ribose configuration was assigned to this compound according to the analogous experiments reported in the pyrimidine nucleosides.[33,34]

When the compound V was refluxed in 1 *N* sodium hydroxide solution for 1 hr., hydrolysis of the 2-chloro atom and cleavage of the imidazole ring occurred. Paper chromatographic experiments showed the existence of a substance assumed to be 2-hydroxy-4,6-diamino-5-thiocarbamylpyrimidine (XII) and a polymerized sugar. Compound XII gave 2-hydroxy-4,5,6-triaminopyrimidine by desulfurization with Raney nickel.

The cleavage reaction of the 8,2′-anhydro linkage with various reagents is now under investigation and will be reported later.

Experimental[35]

2,8-Dichloroadenine Chloromercury Salt (I). This compound was obtained according to Davoll's pro-

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(18) C. D. Jardetzky and O. Jardetzky, *J. Am. Chem. Soc.*, **82**, 222 (1960).

(19) L. M. Jackman, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1959, p. 53.

(20) Although the magnitude of the shift (0.1 p.p.m.) does not coincide with the predicted value (0.2 p.p.m.), the discrepancy may be ascribed to the deformation of furanose ring.[18,21]

(21) R. U. Lemieux, *Can. J. Chem.*, **39**, 116 (1961).

(22) J. Davoll and B. A. Lowy, *J. Am. Chem. Soc.*, **74**, 1563 (1952).

(23) H. Venner, *Chem. Ber.*, **93**, 140 (1960).

(24) A. R. Todd and T. L. V. Ulbricht, *J. Chem. Soc.*, 3275 (1960).

(25) Purchased from Sigma Chemical Co., St. Louis, Mo.

(26) J. G. Buchanan, *Nature*, **168**, 1091 (1951).

(27) S. M. Partridge, *ibid.*, **164**, 443 (1949).

(28) N. C. Yung and J. J. Fox, *J. Am. Chem. Soc.*, **83**, 3060 (1961).

(29) The relatively unstable anhydro linkage of pyrimidine cyclonucleoside may be explained by the deformation of pyrimidine ring as having partially zwitterionic nature.[30]

(30) K. C. Murdock and R. B. Angier, *J. Am. Chem. Soc.*, **84**, 3784 (1962).

(31) This component gave an ultraviolet absorption like 2-chloro-8-oxyadenine. This fraction may be a mixture of compound V and 2-chloro-8-oxy-9-(2′-deoxy-2′-mercapto)arabinofuranosyladenine or its disulfide.

(32) M. Ikehara, H. Tada, and K. Muneyama, following paper of this series.

(33) D. G. Brown, D. B. Parihar, C. B. Reese, and A. R. Todd, *J. Chem. Soc.*, 3035 (1958).

(34) J. F. Codington, I. Doerr, D. V. Praag, A. Bendich, and J. J. Fox, *J. Am. Chem. Soc.*, **83**, 5030 (1961).

(35) Ultraviolet absorption spectra were taken with a Beckman DK-II or Hitachi EPS-2U automatic recording spectrophotometer. Infrared absorption spectra were taken with a JASCO DS-301 spectrophotometer. N.m.r. spectra were taken with a Varian V-4300 C high-resolution spectrophotometer operating at 60 Mc. Tetramethylsilane was used as an internal reference.

cedure[36] with slight modification. 2,8-Dichloroadenine (2.0 g.) was suspended in 100 ml. of water at 80° and 20 ml. of 0.5 *N* sodium hydroxide solution was added with stirring. To the clear stirred solution, 2.7 g. of mercuric chloride dissolved in *ca.* 50 ml. of ethanol was added. After allowing to stand for 1 hr., a white precipitate was collected by centrifugation. The precipitate was washed with 50% ethanol, then ethanol, and finally with ether and dried over phosphorus pentoxide for 5 hr. at 100° under 3 mm., yielding 2.5 g. (58.1%).

*2,8-Dichloro-9-(2′-O-acetyl-3′-O-tosyl-5′-O-methoxycarbonyl)-β-*D*-xylofuranosyladenine (III).* 2,8-Dichloroadenine chloromercury salt (14.8 g.) was suspended in 600 ml. of dry xylene, and a dry benzene (100 ml.) solution of 2-*O*-acetyl-3-*O*-tosyl-5-*O*-methoxycarbonyl-D-xylofuranosyl chloride (II)[14] (freshly prepared from 14.4 g. of 1,2-*O*-isopropylidene-3-*O*-tosyl-5-*O*-methoxycarbonyl-D-xylofuranose) was added. Traces of water were removed by azeotropic distillation with 150 ml. of xylene. After reflux for 75 min. a yellow solution was obtained, which was concentrated to a small volume *in vacuo*. The residual sirup was dissolved in chloroform (300 ml.), the small amount of insoluble product was filtered, and the chloroform layer was washed with potassium iodide solution and water. Evaporation of the dried (sodium sulfate) chloroform solution gave a pale yellow glass (12.3 g., 68%), which was crystallized from benzene. The crude product, m.p. 70–80°, was recrystallized from ethanol and gave colorless long needles; m.p. 160–162° (yield 5.3 g., 26.8%); ultraviolet absorption $\lambda_{\max}^{0.1N\,\mathrm{HCl}}$ 267.5 mμ, $\lambda_{\max}^{0.N\,\mathrm{NaOH}}$ 268 mμ; paper chromatography, R_f 0.90 (*n*-butyl alcohol–water, 86:14); $[\alpha]^{20.5}\mathrm{D}$ −26.0° (*c* 1.0, chloroform).

*2-Chloro-8-mercapto-9-(2′-O-acetyl-3′-O-tosyl-5′-O-methoxycarbonyl)-β-*D*-xylofuranosyladenine (IV).* 2,8-Dichloro-9-(2′-*O*-acetyl-3′-*O*-tosyl-5′-*O*-methoxycarbonyl)-β-D-xylofuranosyladenine (III) (500 mg.) was refluxed in 30 ml. of anhydrous *n*-butyl alcohol with 200 mg. (3.1 molar equiv.) of thiourea for 8 hr. The solvent was removed *in vacuo* and the residue was dissolved in chloroform. The chloroform layer was washed thoroughly with water. The hard sirup obtained after removal of the solvent was dried for 5 hr. at 3 mm. over phosphorus pentoxide: yield 460 mg., 92.4%; ultraviolet absorption $\lambda_{\max}^{0.11N\,\mathrm{HCl}}$ 302 and 310 mμ, $\lambda_{\max}^{0.1N\,\mathrm{NaOH}}$ 300 mμ; paper chromatography, R_f 0.90 (*n*-butyl alcohol–water, 86:14).

*8,2′-Anhydro-2-chloro-8-mercapto-9-β-*D*-arabinofuranosyladenine (V).* 2-Chloro-8-mercapto-9-(2′-*O*-acetyl-3′-*O*-tosyl-5′-*O*-methoxycarbonyl)-β-D-xylofuranosyladenine (2.50 g.), obtained as above, was dissolved in a solution of anhydrous methanol (240 ml.) containing 300 mg. (3.1 equiv.) of metallic sodium. The solution was refluxed for 12 min. After cooling, 10 ml. of Amberlite IRC-50 (H^+ form) was added and the mixture was shaken for 1 hr. After the removal of resin by filtration, the filtrate and washings were combined and evaporated *in vacuo* to a glass. Recrystallization from water gave colorless needles; m.p. 228–229° (yield 550 mg., 41.0%); ultraviolet absorption $\lambda_{\max}^{0.1N\,\mathrm{HCl}}$ 281.5 mμ (ε 2.21 × 10^4), $\lambda_{\max}^{\mathrm{H_2O}}$ 279 mμ (ε 2.2 × 10^4), $\lambda_{\max}^{0.1N\,\mathrm{NaOH}}$ 281 mμ (ε 2.11 × 10^4); infrared absorption band ($\nu_{\max}^{\mathrm{Nujol}}$ 863 cm.$^{-1}$) was not detected; n.m.r. absorption band, doublet at 409 c.p.s. ($C^{1'}$ proton); coupling constant, 7 c.p.s.; $[\alpha]^{20.5}\mathrm{D}$ −214 (*c* 1.0, water)[37]; paper chromatography, R_f 0.42, R_{Ad}[38] 1.10 (water, pH 10.0).

2-Chloro-2′-deoxyadenosine (VII). 8,2′-Anhydro-2-chloro-8-mercapto-9-β-D-arabinofuranosyladenine (520 mg.) was dissolved in 50 ml. of 50% (v./v.) ethanol and refluxed with 1 ml. (wet) of Raney nickel[39] for 1.5 hr. The ultraviolet absorption maximum of the reaction mixture shifted from 277 to 264 mμ. After removal of Raney nickel by filtration, the filtrate and washings were combined and evaporated *in vacuo*. A pale yellow glass was obtained (263 mg., 57.6%); paper chromatography, R_f 0.52 (water, pH 10.0). This spot was visualized by an ultraviolet lamp and excized from the paper chromatogram; ultraviolet absorption properties $\lambda_{\max}^{0.1N\,\mathrm{HCl}}$ 265 mμ, $\lambda_{\max}^{0.1N\,\mathrm{NaOH}}$ 265 mμ. The sample revealed a pink color (490 mμ) with Dische's reagent.[24]

2′-Deoxyadenosine (VIII). 2′-Chloro-2′-deoxyadenosine (263 mg.), obtained as above, was dissolved in 50 ml. of water and 3 ml. of aqueous ammonia (28%) was added. Freshly prepared 20% palladized charcoal (400 mg.) was added and shaken for 30 min. with hydrogen. The hydrogen uptake[40] ceased after the absorption of 22 ml. Removal of the catalyst by filtration and evaporation of solvent gave a colorless glass. Recrystallization from water gave material with m.p. 185–189° (50 mg.). The physical properties compared with an authentic sample of natural 2′-deoxyadenosine are listed in Table I. This specimen was definitely different from synthetic 3′-deoxyadenosine.[2]

Alkaline Hydrolysis of V. (*a*). Compound V (10 mg.) was refluxed in 5 ml. of 0.5 *N* sodium hydroxide for 2 hr. Examination of the reaction mixture showed $\lambda_{\max}$ 279 mμ similar to that of V (R_f 0.42). (*b*). Compound V (10 mg.) was refluxed in 5 ml. of 1 *N* sodium hydroxide for 60 min. Paper chromatography (pH 10, water) of the reaction mixture showed two spots having R_f values of 0.55 (ultraviolet absorbing) and 0.10 (metaperiodate consuming) (cochromatographed V had R_f 0.64). Ultraviolet absorption spectra of the reaction mixture showed $\lambda_{\max}^{0.1N\,\mathrm{NaOH}}$ 292 mμ, $\lambda_{\mathrm{shoulder}}^{0.1N\,\mathrm{NaOH}}$ 263 mμ; $\lambda_{\max}^{1.0N\,\mathrm{HCl}}$ 260 and 300 mμ. The above reaction mixture was refluxed with Raney nickel (*ca.* 0.5 ml.) for 1 hr. and examined by paper chromatography (water, pH 10.0), R_f 0.61; cochromatographed adenine 0.39, 2-chloroadenine 0.31; ultraviolet absorption properties of spot of R_f 0.61, $\lambda_{\max}^{0.1N\,\mathrm{NaOH}}$ 282 mμ, $\lambda_{\max}^{0.1N\,\mathrm{HCl}}$ 281 mμ, This was similar with those of 2-hydroxy-4,5,6-triaminopyrimidine.[41]

Acidic Hydrolysis of V. (*a*). Compound V (14 mg.) was refluxed in 0.2 *N* sulfuric acid (2.5 ml.) for 60 min. Paper chromatography (*n*-butyl alcohol–acetic acid–water, 4:1:5) showed R_f 0.60, same as V;

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(36) J. Davoll and B. Lowy, *J. Am. Chem. Soc.*, **73**, 1650 (1951).

(37) The unusually large levorotation is noteworthy.

(38) R_{ad} stands for the value obtained from the R_f of V divided by R_f of cochromatographed adenosine.

(39) R. Mozingo, D. E. Wolf, S. A. Harris, and K. Folkers, *J. Am. Chem. Soc.*, **65**, 1013 (1943).

(40) To promote initiation of hydrogen uptake, a few milligrams of platinum oxide was added.

(41) M. M. Stimson, *J. Am. Chem. Soc.*, **71**, 1470 (1949).

Table II

Solvent	R_f	Ultraviolet absorption properties, mμ		IO_4^- consumption[a]
Water (pH 10.0)	0.58	$\lambda_{max}^{H_2O}$ 292		−
	0.46	$\lambda_{max}^{H_2O}$ 290		+
	0.39	$\lambda_{max}^{H_2O}$		+
Isopropyl alcohol–ammonia–water, 7:1:2	0.65			−
	0.39			+
	0.19			−
	0.10–0.15	fluorescent		+
	0.67[b]			
Butanol–water, 86:14	0.61	λ_{max}^{EtOH} 298,	$\lambda_{max}^{0.1N NaOH}$ 304	+
	0.28			±
	0.09	λ_{max}^{EtOH} 308,	$\lambda_{max}^{0.1N NaOH}$ 303–304	±
Butanol–acetic acid–water, 4:1:5	0.80	$\lambda_{max}^{0.1N HCl}$ 288,	$\lambda_{max}^{0.1N NaOH}$ 299	±
	0.62	$\lambda_{max}^{0.1N HCl}$ 274,	$\lambda_{max}^{0.1N NaOH}$ 290	±
	0.53	λ_{max}^{EtOH} 280,	$\lambda_{max}^{0.1N NaOH}$ 285	−
	0.08	$\lambda_{max}^{H_2O}$ 303,	$\lambda_{max}^{0.1N NaOH}$ 305	+

[a] + means definite consumption of metaperiodate, ± means very slight consumption, and − means no consumption. [b] *Rf* values of compound V.

ultraviolet absorption of the 50% ethanol extract of the spot (λ_{max} 282.5 mμ) was similar to V. (*b*). Compound V (11 mg.) was refluxed in 2 *N* sulfuric acid (2 ml.) for 100 min. The reaction mixture was examined by paper chromatography in four solvent systems indicated in Table II.

The substance having R_f 0.80 in solvent butanol–acetic acid–water was collected by evaporation of water extracts of the zone having R_f 0.80 excised from the preparative paper chromatogram and refluxed in water with Raney nickel (*ca.* 0.2 ml.). Ultraviolet absorption maximum was changed to 265 mμ. This was identical with that of 2-chloroadenosine and 2-chloro-2′-deoxyadenosine; paper chromatography (water, pH 10.0), R_f 0.69, cochromatographed adenosine 0.55, compound V 0.38, adenine 0.55, 2-chloroadenine 0.31, and 2-chloro-8-mercaptoadenine 0.51. The first two spots consumed metaperiodate.

The substance having R_f 0.53 (butanol–acetic acid–water) was collected as above and reduced with hydrogen over palladized charcoal catalyst (20%, 10 mg.). The catalyst was removed by filtration and the filtrate was evaporated *in vacuo*. Ultraviolet absorption of this material gave $\lambda_{max}^{0.1N HCl}$ 272 mμ, $\lambda_{max}^{0.1N NaOH}$ 276 mμ. This was identical with that of 8-hydroxyadenine synthesized by the reported procedure.[42]

The substance having R_f 0.08 (butanol–acetic acid–water) was collected by the same procedure. The ultraviolet spectra of this material gave $\lambda_{max}^{H_2O}$ 303 mμ, $\lambda_{max}^{0.1N HCl}$ 311 mμ, $\lambda_{max}^{0.1N NaOH}$ 305 mμ; R_f (water pH 10.0) was 0.46, cochromatographed adenine 0.37, 2-chloro-8-mercaptoadenine 0.46. The spot having R_f 0.46 consumed metaperiodate.

The yield of the compound obtained by preparative paper chromatography was estimated by optical density: 2-chloro-9-ribosyladenine-(8)-disulfide (mol. wt. 525.4, ε 14,000), 27.3%; 2-chloro-8-hydroxyadenine (mol. wt. 185.6, ε 13,000), 22.9%; 2-chloro-8-mercaptoadenine (mol. wt. 201.6, ε 18,000), 20.1%.

2-Chloro-8-mercaptoadenine. 2,8-Dichloroadenine (100 mg.) and thiourea (100 mg., 2.6 equiv.) was dissolved in ethanol (25 ml.) and heated at 160–180° for 8 hr. in a sealed tube. The crystalline substance was collected by filtration and washed with ethanol. Yellow crystals, m.p. 280°, were obtained, yield *ca.* 100 mg.; ultraviolet absorption $\lambda_{max}^{H_2O}$ 297 and 304 mμ; $\lambda_{max}^{0.1N HCl}$ 297 and 304 mμ; $\lambda^{0.1N NaOH}$ 300 mμ; paper chromatography (isopropyl alcohol–ammonia–water, 7:1:2), R_f 0.47, dichloroadenine 0.65; water (pH 10.0) 0.51, adenine 0.38.

Anal. Calcd. for $C_5H_4ClN_5S\cdot 0.5H_2O$: N, 33.4. Found: N, 33.08.

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