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Synthesis of 2- and 8-Cyanoadenosines and Their Derivatives (Nucleosides and Nucleotides. XXVII[1])

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A facile displacement of a methylsulfonyl group in adenosines with cyanide ion is described. Treatment of protected 8-methylsulfonyladenosines with sodium cyanide in dimethylformamide gave the 8-cyanoadenosines. The conversion of the cyano group to the methyl imidate, methoxycarbonyl, carbamoyl, and carboxylic acid, respectively, was achieved. Similar reaction was carried out with 2-methylsulfonyladenosines to give the 2-cyanoadenosines and their derivatives. The nuclear magnetic resonance (NMR) and circular dichroism (CD) spectra of these 2- and 8-substituted adenosines are given. The 8-substituted adenosines possess *syn*-conformations while the 2-substituted derivatives prefer to possess *anti*-conformations, as confirmed by the CD and NMR spectra.

Keywords——adenosine derivatives; nucleophilic substitution; sodium cyanide; NMR; UV; CD; nucleoside conformations

In the continuing studies of the conversion of the purine moiety in adenosine[3] the study of the synthesis of C-alkylated derivatives of adenosine was undertaken. The formation of the carbon-carbon bond at the 2- and 8-positions of purine nucleoside through the nucleophilic displacement of the corresponding halogenopurine nucleosides has been generally unfruitful. The carbon-substituted purine nucleosides at the 2-position have been prepared by the ring closure of aminoimidazolecarboxamide nucleoside[4] or by the glycosylation of the appropriate purine base.[5] The homolytic alkylations have been applied to the synthesis of 8-methyl[6] and 8-hydroxyalkyl-[7] adenosines. In general, 8-bromoadenosines are useful intermediates for the preparation of the 8-halo-, 8-amino-, and 8-thioadenosines. Attempts to displace the 8-bromo group with carbanions such as cyanide[8] or nitromethyl anion[9] have been unsuccessful except potassium cyanide in the presence of a crown ether.[10] 8-Bromoadenosine 3′,5′-cyclic phosphate was reported to give the 8-carbamoyl derivative by treatment with cyanide ion in dimethylformamide (DMF).[8]

A methylsulfonyl group is known to be a good leaving group in the displacement with carbon nucleophiles in nitrogen-containing heterocycles. For example, 2-methylsulfonylquinoxaline, 4-methylsulfonylcinnoline, and 6-methylsulfonyl-9-phenylpurine afforded the

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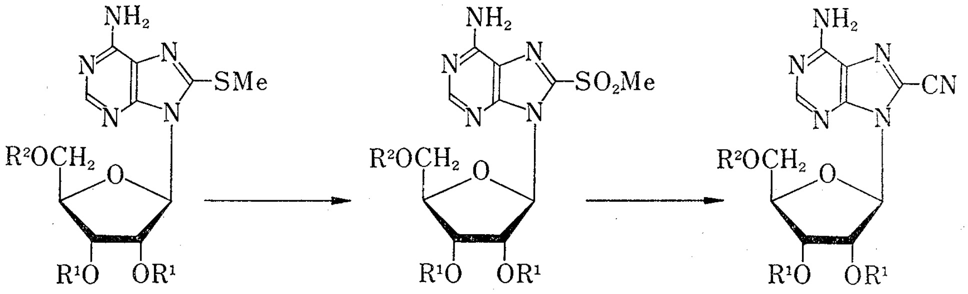
respective carbon-linked heterocycles upon reaction with cyanide ion and other carbanions.[11] 4-Methylsulfonylquinoline gave a quinolyl ylide by the action of diphenylsulfonium methylide.[12] We found that the 8-methylsulfonyladenosine was readily displaced with cyanide ion to give the 8-cyanoadenosine derivative. The derivatization of the 8-cyano group as well as the reaction with 2-methylsulfonyladenosine derivative will also be described.

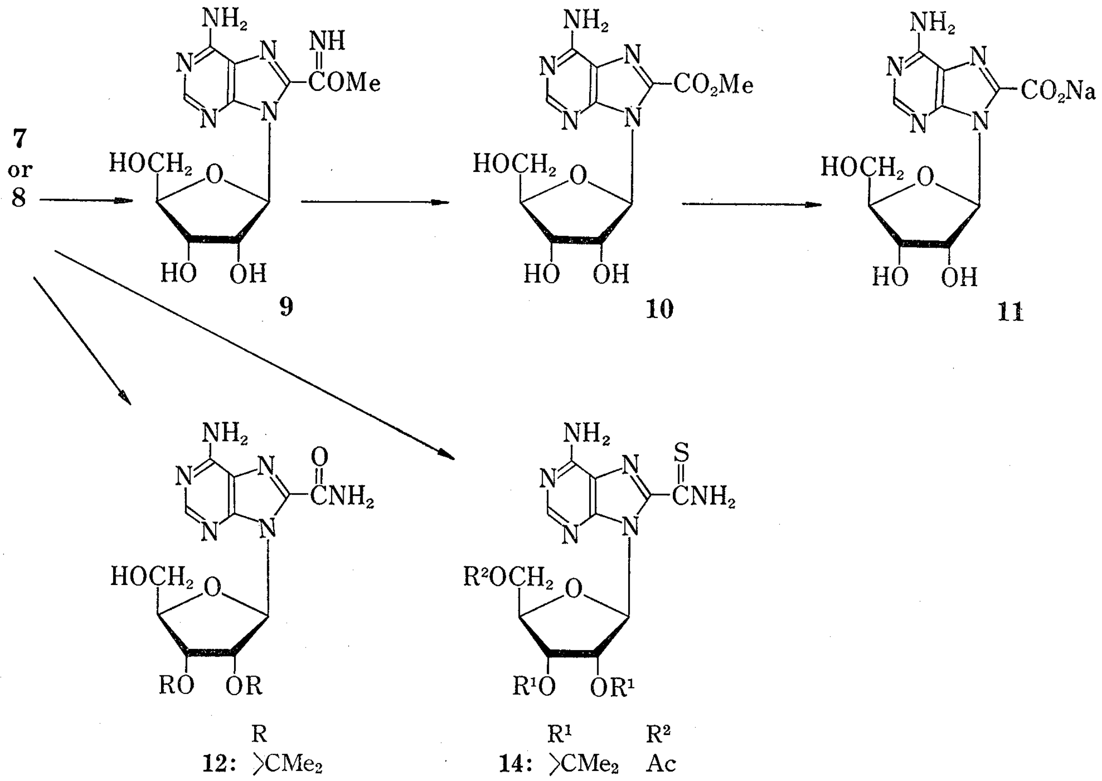


	R^1	R^2
1:	$>CMe_2$	H
2:	H	H
3:	$>CMe_2$	Ac
4:	Ac	Ac

	R^1	R^2
5:	$>CMe_2$	Ac
6:	Ac	Ac

	R^1	R^2
7:	$>CMe_2$	Ac
8:	Ac	Ac

Chart 1



	R
12:	$>CMe_2$
13:	H

	R^1	R^2
14:	$>CMe_2$	Ac
15:	$>CMe_2$	H
16:	Ac	Ac
17:	H	H

Chart 2

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11) *a*) E. Hayashi and T. Miyagishima, *Yakugaku Zasshi*, **87**, 1103 (1967); *b*) E. Hayashi, Y. Akahori, and T. Watanabe, *Yakugaku Zasshi*, **87**, 1115 (1967); *c*) E. Hayashi, N. Shimada, and A. Miyashita, *Yakugaku Zasshi*, **96**, 1370 (1976).

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2′,3′-O-Isopropylidene-8-bromoadenosine[13] and 8-bromoadenosine[14] were converted to the respective 8-methylthio derivatives (**1** and **2**) by a slightly modified procedure of the method described by Holmes and Robins,[14] which were then acetylated to give the 5′-O-acetyl (**3**) and 2′,3′,5′-tri-O-acetyl (**4**) derivatives. Oxidation of **3** and **4** with $KMnO_4$ in 50% acetic acid at 0° afforded the respective 8-methylsulfonyl derivatives (**5** and **6**) in high yields. Treatment of **5** with sodium cyanide in DMF at room temperature for 2 hr gave 2′,3′-O-isopropylidene-5′-O-acetyl-8-cyanoadenosine (**7**) as crystals in quantitative yield. The structure of **7** was confirmed by the detection of a nitrile group in infrared (IR) spectrum ($2250\ cm^{-1}$) and by elemental and mass analyses. The blue-fluorescent properties of **7** under ultraviolet (UV) ray is also characteristic. Treatment of **6** with sodium cyanide in DMF afforded a mixture showing three spots on a thin layer chromatogram. The mixture was separated by a silica gel column, giving 2′,3′,5′-tri-O-acetyl-8-cyanoadenosine (**8**) as a homogeneous powder, 2′,3′,5′-tri-O-acetyl-N^6-acetyl-8-cyanoadenosine, and di-O-acetylated derivatives. In this reaction the presence of cyanide ion seemed to accelerate the O→N acetyl migration.

This facile substitution of the 8-methylsulfonyl group with cyanide ion is to be contrasted with the sluggish reaction starting from the 8-bromo derivative of adenosine.[8] In the

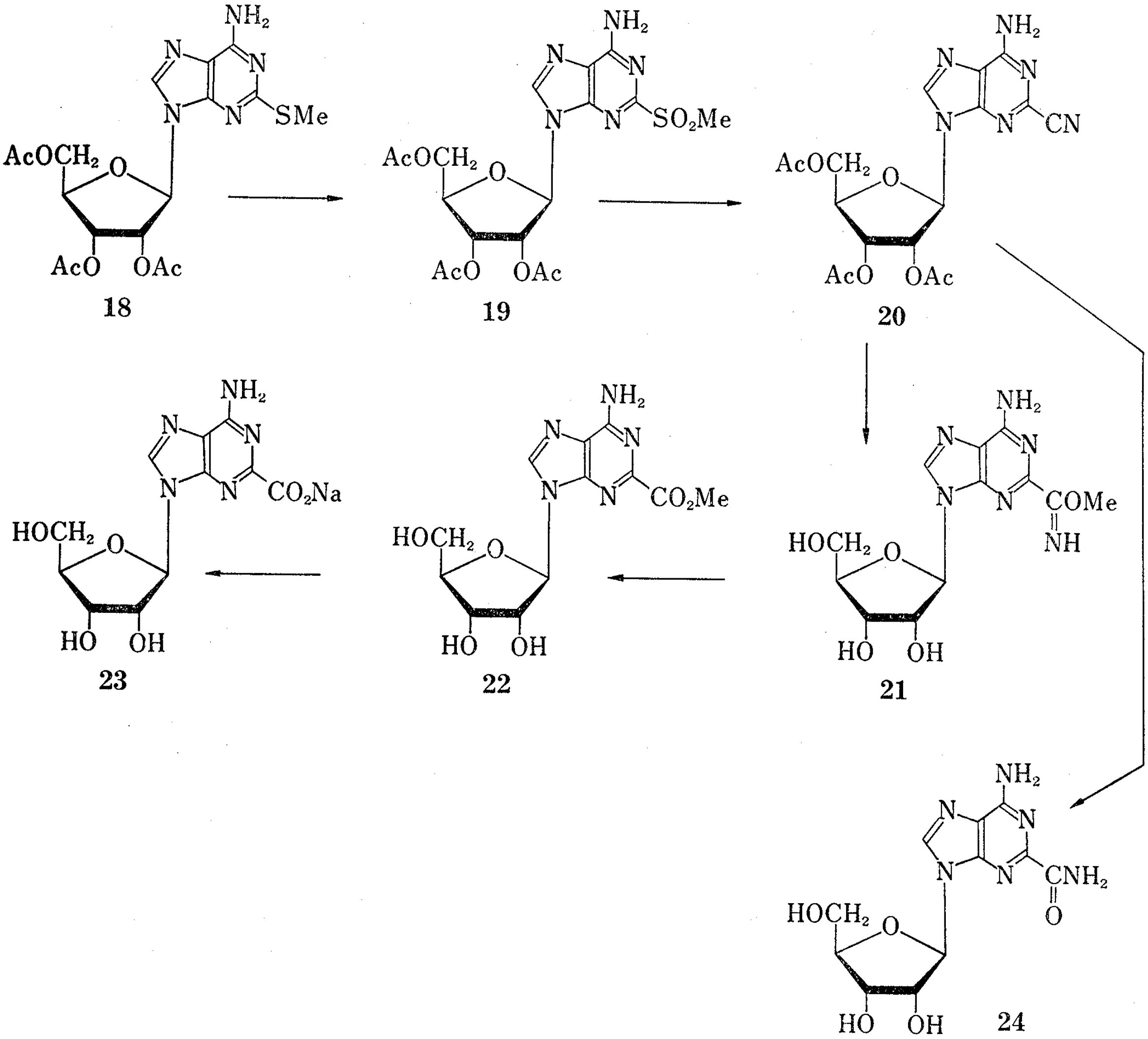

Chart 3

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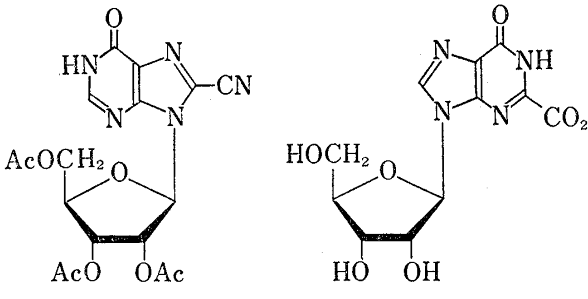
[13] M. Ikehara, H. Tada, and M. Kaneko, *Tetrahedron*, **24**, 3489 (1968).
[14] R.E. Holmes and R.K. Robins, *J. Am. Chem. Soc.*, **86**, 1242 (1964).

substitution at the 8-position of guanosine no such differences have been observed between bromo and methylsulfonyl leaving groups.15) The dissociation of the N^1-proton in the case of guanosine derivatives would have prevented the facile substitution as observed in the adenosine series.

The conversion of the 8-cyano group to the carboxyl group was performed *via* the methyl imidate intermediate, as was done in the conversion of 6-cyanocytidine to cytidine 6-carboxylic acid.16) Treatment of **8** with sodium methoxide in methanol at room temperature overnight afforded methyl adenosine-8-carboximidate (**9**) in 68% yield. The structure of **9** was confirmed by the disappearance of the cyano group in IR spectrum and appearance of a methoxy and an imino protons (2.90 and 9.14 ppm) in NMR spectrum. Compound **9** was readily hydrolyzed in an acidic medium at 0° for 2 hr to give the methyl adenosine-8-carboxylate (**10**) in 88% yield. Subsequent alkaline hydrolysis of **10** furnished adenosine-8-carboxylic acid (**11**). Free acid of **11** was unstable and the decarboxylation occurred readily in a solution of dimethylsulfoxide,8) or even in a crystalline state. Compound **7** and **8** were hydrolyzed in alkaline media to give the respective carboxamides (**12** and **13**). The UV spectra of **12** (and **13**) were closely similar to those of the 3′,5′-cyclic phosphate.8) Treatment of **7** and **8** with hydrogen sulfide in pyridine at 0° afforded the respective 8-thiocarboxamides (**14** and **16**). Deacetylation of the products with sodium methoxide in methanol at room temperature gave the adenosine-8-thiocarboxamides (**15** and **17**).

The displacement of the methylsulfonyl group in the 2-position of adenosine was next undertaken. 2-Methylthioadenosine17) was acetylated and the tri-O-acetate (**18**) was oxidized with $KMnO_4$ to give the 2-methylsulfonyladenosine (**19**) in high yield. Treatment of **19** with sodium cyanide in DMF at 100° for one hr gave a mixture of products from which 2′,3′,5′-tri-O-acetyl-2-cyanoadenosine (**20**) was isolated through a silica gel column in 67% yield as a hemi-hydrate. The formation of tetra- and di-acetate of 2-cyanoadenosine was observed again in this case. Treatment of **20** with sodium methoxide in methanol afforded the 2-carboximidate (**21**) in 89% yield, which was converted to the methyl ester (**22**) by treatment with acid at room temperature. Compound **22** was hydrolyzed in an alkaline medium to give adenosine-2-carboxylic acid (**23**). Treatment of **20** with alkaline solution afforded the 2-carboxamide (**24**) of adenosine.

The behaviors of cyanoadenosines (**8** and **20**) toward deamination by nitrous acid are different. Treatment of **8** with sodium nitrite in 90% acetic acid aforded the deaminated product, 2′,3′,5′-tri-O-acetyl-2-cyanoinosine (**25**), whereas a similar treatment of **20** gave, after deacetylation, inosine-2-carboxylic acid (**26**). Since compound **20** is stable in 90% acetic acid, the initially deaminated 2-cyanoinosine acetate would undergo rapid hydrolysis (to the 2-carboxamide) and deamination to give the tri-acetate of **26**.



25 **26**

Chart 4

The glycosylic linkages of purine nucleosides are generally acid-labile. The effect of the cyano group on this lability was investigated. Treatment of adenosine, **13** and **24** in 1 N hydrochloric acid at 37° for 24 hr resulted in the formation of adenine (62%), adenine-8-carboxamide (100%), and adenine-

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Table I. Proton Chemical Shifts of 2-and 8-Substituted Adenosines

	Adenosine	**9**	**10**	**11**	**13**	**17**	**21**	**22**	**23**	**24**
2-H	8.15	8.17	8.22	8.07	8.18	8.15				
8-H	8.35						8.48	8.53	8.38	8.49
1′-H	5.87	6.05	6.65	6.96	6.86	6.40	5.93	5.94	5.97	5.97
2′-H	4.59	4.90	5.28	4.80	4.93	4.88	4.60	4.57	4.57	4.61
3′-H	4.16	4.16	4.24	4.20	4.20	4.19	4.21	4.14	4.18	4.17
4′-H	3.99	3.90		3.98	3.89	3.97	4.04	3.95	4.02	3.97
5′-H	3.36	3.54	3.95	3.63	3.68	3.67	3.66	3.64	3.67	3.66
OMe		3.90					3.84	3.84		

Measured in DMSO-d_6–D_2O at 30°, as expressed by δ (ppm) with 100 MHz.

2-carboxamide (78%), respectively, as determined by paper chromatography of each hydrolyzate. The glycosylic linkage of the 8-substituted adenosine was found to be the weakest. The pK_a values of **13** and **24** were determined by the photometric method as 3.4 and 2.6, respectively. It is rational that the protonation of the N^1 position of adenosine would be suppressed by the introduction of a cyano group in the 2-position rather than in the 8-position.

Some spectroscopic nature of the 2- and 8-substituted adenosines prepared in the present study is to be mentioned. The chemical shifts in NMR spectra of the compounds (**9**, **10**, **11**, **13**, **17**, **21**—**24**) are shown in Table I. The chemical shifts of 1′- and 2′-protons of the 8-substituted derivatives shifted down field as compared with those of adenosine whereas those of the 2-substituted derivatives stayed within the same range. The large down field shifts of the 2′-protons in the 8-substituted derivatives can be attributed to the *syn*-conformations of these nucleosides in which the deshielding anisotropy of the N^3-electrons to the 2′-protons was effective.[18] The large down field shifts of the anomeric protons of these compounds may be due to the deshielding effect of the carbonyl group in **10**, **11**, and **13**, and an imino and a thione group in **9** and **17**, respectively. The C–H bond polarization of the anomeric protons caused by an electric field effect of the 8-substituents may be the alternative effect. The UV absorption maxima of these 8-substituted compounds exhibited large bathochromic shifts as compared with the parent nucleoside, adenosine, indicating the conjugation between the adenine ring and the 8-substituents. It is to be reminded that, in orotidine (uridine-6-carboxylic acid) the plane of the carboxyl group is essentially perpendicular to that of uracil moiety owing to the steric hindrance between the 6-carboxyl and the 1′-proton. In this case such large downfield shift of the 1′-proton signal was not expected as it was found to be the case.[19]

The circular dichroism (CD) and UV spectra of 2- and 8-substituted adenosines are shown in Fig. 1 and 2. In conformity with the general relationship between the sign of the CD band and *syn-anti* conformations,[20] the 2-substituted adenosines (**21**, **22**, **24**) exhibited negative CD bands at the main absorption region, as the preferred *anti*-conformers. By contrast, the 8-substituted adenosines (**9**, **10**, **13**) showed positive CD bands around 260 nm, showing the *syn*-preference in their conformations. These assumptions were in good consistence with the results obtained from the NMR interpretations. The small negative bands observed with **9** and **10** around 290—300 nm may be arosen by certain n-π* transitions of their heterocycles. The molar ellipticities of all compounds measured were below 10^4 which

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19) F.E. Hruska, *J. Am. Chem. Soc.*, **93**, 1795 (1971).

20) See, for example, H. Tanaka, T. Takahashi, H. Togashi, and T. Ueda, *Chem. Pharm. Bull.* (Tokyo), **26**, 3322 (1978), and references therein.

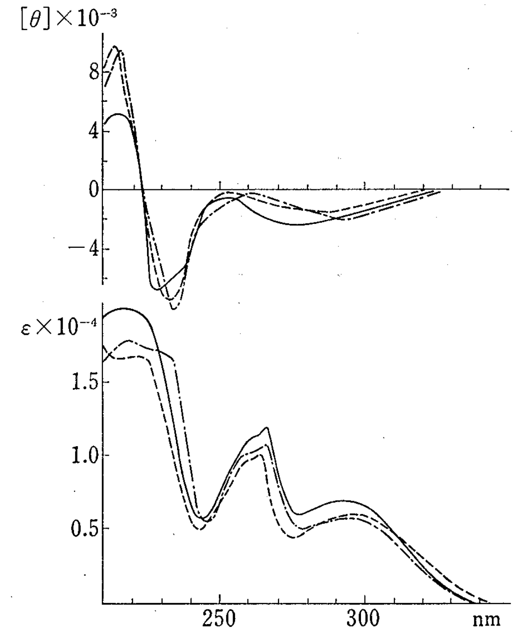

Fig. 1. CD and UV Spectra of 2-Substituted Adenosines

—·—·—: 21, ---------: 22, ————, 24.

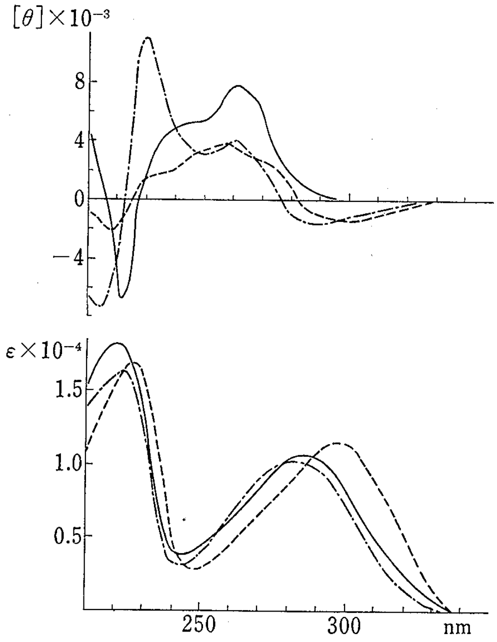

Fig. 2. CD and UV Spectra of 8-Substituted Adenosines

—·—·—: 9, ---------: 10, ————: 13.

would mean that the rotation around the glycosylic linkages is unrestricted for the interconversions of *syn* and *anti* conformers.

Experimental

Melting points were determined with a Yanaco MP-3 melting point apparatus and are uncorrected. UV spectra were recorded on a Shimadzu UV-300 recording spectrophotometer. NMR spectra were taken with a JEOL JNM-FX 100FT NMR spectrometer. IR spectra were recorded on a Hitachi 215 grating infra-red spectrophotometer. Mass spectra were taken with a Hitachi RMU-6E mass spectrometer. CD spectra were recorded on a JASCO J-40 spectropolarimeter with a data processor of 8 accumulations at room temperature.

2′,3′-O-Isopropylidene-8-methylthioadenosine (1)——A mixture of 2′,3′-O-isopropylidene-8-bromoadenosine[13] (5.0 g, 12.9 mmol) and 25% solution of NaSMe (10.3 g, 25.8 mmol) in 50 ml of DMF was stirred for 2 hr at room temperature. The solution was neutralized with 1 N HCl under bubbling of N_2 gas and was evaporated to dryness. The residue was crystallized from EtOH–H_2O to afford 4.0 g (88%) of **1**, mp 215—216°. *Anal.* Calcd. for $C_{14}H_{19}N_5O_4S$: C, 47.68; H, 5.41; N, 19.93; S, 9.21. Found: C, 47.59; H, 5.44; N, 19.83; S, 9.07. UV $\lambda_{max}^{H_2O}$ nm (ε): 280 (18900), λ_{min} 245 (4200), $\lambda_{max}^{1N\ HCl}$ 282 (19700), λ_{min} 243 (4000). $\lambda_{max}^{1N\ NaOH}$ 279 (19100), λ_{min} 245 (4700); MS *m/e*: 353 (M^+); NMR (DMSO-d_6), δ: 8.18 (s, 1, 2-H), 7.28 (bs, 2, NH_2), 6.00 (d, 1, 1′-H), 5.64 (dd, 1, 2′-H), 5.27 (t, 1, 5′-OH), 5.05 (dd, 1, 3′-H), 4.20 (m, 1, 4′-H), 3.56 (m, 2, 5′-H), 2.76 (s, 3, SMe), 1.58, 1.34 (s, 3+3, CMe_2); $J_{1',2'}=3$ Hz, $J_{2',3'}=7$ Hz, $J_{3',4'}=4$ Hz; CD (H_2O): $[\theta]_{285}$ −2800, $[\theta]_{263}$ −600, $[\theta]_{251}$ −2000, $[\theta]_{244}$ 0, $[\theta]_{233}$ +2800, $[\theta]_{224}$ 0, $[\theta]_{215}$ −8200.

2′,3′-O-Isopropylidene-5′-O-acetyl-8-methylthioadenosine (3)——To a solution of **1** (3.4 g, 9.6 mmol) in 100 ml of pyridine was added 20 ml of acetic anhydride and the solution was stirred for 2.5 hr at room temperature. After adding H_2O the solution was evaporated. The evaporation with H_2O was repeated several times and the final residue was crystallized from EtOH–H_2O to afford 2.9 g (76%) of 3, mp 56°. *Anal.* Calcd. for $C_{16}H_{21}N_5O_5S$: C, 48.59; H, 5.36; N, 17.71; S, 8.11. Found: C, 48.59; H, 5.36; N, 17.70; S, 8.17. MS *m/e*: 395 (M^+); NMR (DMSO-d_6) δ: 8.10 (s, 1, 2-H), 7.24 (bs, 2, NH_2), 5.98 (d, 1, 1′-H), 5.63 (dd, 1, 2′-H), 5.08 (dd, 1, 3′-H), 4.23 (m, 3, 4′,5′-H), 2.73 (s, 3, SMe), 1.95 (s, 3, Ac), 1.54, 1.33 (s, 3+3, CMe_2); $J_{1',2'}=2.2$ Hz, $J_{2',3'}=6.3$ Hz, $J_{3',4'}=3.4$ Hz.

8-Methylthioadenosine (2)——A mixture of 8-bromoadenosine[14] (14.8 g, 42.8 mmol) and 25% solution of NaSMe (34.2 g, 85.6 mmol) in 100 ml of DMF was stirred for one hr at room temperature. The solution was neutralized with 1 N HCl under bubbling of N_2 gas and was evaporated to dryness. The residue was crystallized from H_2O to give 10.6 g (79%) of 2, mp 230—233° (ref. 237—238°[14]).

2′,3′,5′-Tri-O-acetyl-8-methylthioadenosine (4)——To a solution of 2 (5.0 g, 16 mmol) in pyridine (75 ml) was added acetic anhydride (12.5 ml) and the solution was stirred for 2.5 hr at room temperature. After adding H_2O the solution was evaporated. The evaporation with H_2O was repeated several times and the final residue was crystallized from EtOH to give 6.3 g (89%) of **4**, mp 168—169°. *Anal.* Calcd. for $C_{17}H_{19}N_5O_7S$: C, 46.46; H, 4.82; N, 15.94; S, 7.30. Found: C, 46.35; H, 4.80; N, 15.91; S, 7.25. UV $\lambda_{max}^{H_2O}$ nm (ε): 280 (17900), λ_{min} 248 (4700), $\lambda_{max}^{1N\ HCl}$ 281 (18800), λ_{min} 243 (2600); MS *m/e*: 439 (M^+); NMR ($CDCl_3$), δ: 8.26 (s, 1, 2-H), 6.24 (dd, 1, 2′-H), 6.06 (d, 1, 1′-H), 5.87 (m, 1, 3′-H), 5.63 (bs, 2, NH_2), 4.41 (m, 3, 4′,5′-H), 2.74 (s, 3, SMe), 2.14, 2.08, 2.05 (s, 3+3+3, Ac_3); CD (H_2O): $[\theta]_{278}$ −5100, $[\theta]_{246}$ 0, $[\theta]_{230}$ +4200, $[\theta]_{221}$ 0, $[\theta]_{212}$ −10800, (0.1 N HCl): $[\theta]_{275}$ 0, $[\theta]_{245}$ −1500, $[\theta]_{234}$ 0, $[\theta]_{221}$ +6300, $[\theta]_{215}$ 0, $[\theta]_{208}$ −13800.

2′,3′-O-Isopropylidene-5′-O-acetyl-8-methylsulfonyladenosine (5)——To a solution of 3 (2.9 g, 7.3 mmol) in 50% acetic acid (50 ml) was added $KMnO_4$ (2.2 g, 14 mmol) in an ice-bath and the mixture was stirred for 2 hr. To a colored suspension obtained was added 35% H_2O_2 until it became colorless and the precipitate was collected by filtration. The filtrate and washings were combined and extracted with $CHCl_3$. The $CHCl_3$ layer was evaporated and the residue and the precipitate were combined, and crystallized from EtOH–H_2O to afford 2.5 g (80%) of **5**, mp 186—187°. *Anal.* Calcd. for $C_{16}H_{21}N_5O_7S$: C, 44.96; H, 4.97; N, 16.39; S, 7.49. Found: C, 45.24; H, 4.89; N, 16.12; S, 7.56. UV $\lambda_{max}^{H_2O}$ nm (ε): 284 (12200), 221 (19000), λ_{min} 249 (4200), $\lambda_{max}^{1N\ HCl}$ 270 (15900), λ_{min} 235 (3200); MS *m/e*: 427 (M^+); NMR (DMSO-d_6), δ: 8.30 (s, 1, 2-H), 7.91 (bs, 2, NH_2), 6.69 (s, 1, 1′-H), 5.67 (dd, 1, 2′-H), 5.13 (dd, 1, 3′-H), 4.30 (m, 3, 4′,5′-H), 3.55 (s, 3, SO_2Me), 1.94 (s, 3, Ac), 1.54, 1.33 (s, 3+3, CMe_2); $J_{1',2'}=2$ Hz, $J_{2',3'}=2$ Hz, $J_{3',4'}=3.2$ Hz; CD (H_2O): $[\theta]_{286}$ −3000, $[\theta]_{271}$ −1700, $[\theta]_{255}$ −4600, $[\theta]_{235}$ −400, $[\theta]_{222}$ −10700, $[\theta]_{210}$ 0, $[\theta]_{200}$ +4200.

2′,3′,5′-Tri-O-acetyl-8-methylsulfonyladenosine (6)——To a solution of **4** (1.0 g, 2.3 mmol) in 50%acetic acid (30 ml) was added $KMnO_4$ (1.0 g, 6.3 mmol) in an ice-bath and the mixture was stirred for one hr at 0°. A solution of 35% H_2O_2 was added to decolorize the mixture, and the clear solution was extracted with $CHCl_3$. The organic layer was dried over Na_2SO_4 and evaporated. The residue was crystallized from EtOH–H_2O to give 0.7 g (65%) of **6**, mp 227—228°. *Anal.* Calcd. for $C_{17}H_{21}N_5O_9S$: C, 43.31; H, 4.46; N, 14.86; S, 6.79. Found: C, 43.60; H, 4.52; N, 14.88; S, 6.90. UV $\lambda_{max}^{H_2O}$ nm (ε): 284 (12400), 221 (20300), λ_{min} 246 (2500), $\lambda_{max}^{1N\ HCl}$ 269 (16800), λ_{min} 234 (3000); NMR (DMSO-d_6), δ: 8.30 (s, 1, 2-H), 7.85 (bs, 2, NH_2), 6.60 (s, 1, 1′-H), 6.26 (dd, 1, 2′-H), 5.95 (m, 1, 3′-H), 4.40 (m, 3, 4′,5′-H), 3.45 (s, 3, SO_2Me), 2.11, 2.05, 1.94 (s, 3+3+3, Ac_3); $J_{1',2'}=4$ Hz, $J_{2',3'}=6$ Hz; CD (H_2O): $[\theta]_{285}$ −1200, $[\theta]_{270}$ −900, $[\theta]_{265}$ −1000, $[\theta]_{237}$ 0, $[\theta]_{223}$ +2100; (0.1 N HCl): $[\theta]_{310}$ −700, $[\theta]_{270}$ 0, $[\theta]_{240}$ −1400, $[\theta]_{227}$ 0, $[\theta]_{220}$ +1000, $[\theta]_{214}$ 0, $[\theta]_{205}$ −3100.

2′,3′-O-Isopropylidene-5′-O-acetyl-8-cyanoadenosine (7)——To a solution of **5** (2.56 g, 6 mmol) in 10 ml of DMF was added NaCN (0.45 g, 9 mmol) and the solution was stirred for 2 hr at room temperature. The solution was adjusted to pH 7 with 1 N HCl and was partitioned with AcOEt and H_2O. The organic layer was dried over Na_2SO_4 and evaporated to leave a residue, which was taken in $CHCl_3$ and applied to a column of silica gel (3.7 × 12 cm). After washing the column with $CHCl_3$ it was eluted with 2% EtOH in $CHCl_3$. The eluate was evaporated and the residue was crystallized from ether to give 2.25 g (100%) of **7**, mp 130—132°. *Anal.* Calcd. for $C_{16}H_{18}N_6O_5$: C, 51.33; H, 4.85; N, 22.45. Found: C, 51.27; H, 4.89; N, 22.45. UV $\lambda_{max}^{H_2O}$ nm (ε): 299 (13000), 276 (sh, 8600), 269 (sh, 6600), 230 (19200), λ_{min} 245 (2600), $\lambda_{max}^{1N\ HCl}$ 294 (sh, 12000), 285 (16800), 276 (sh, 16000), λ_{nim} 241 (3200); IR (KBr): 2250 cm^{-1} (CN); MS *m/e*: 374 (M^+); NMR (DMSO-d_6), δ: 8.31 (s, 1, 2-H), 7.99 (bs, 2, NH_2), 6.20 (s, 1, 1′-H), 5.73 (dd, 1, 2′-H), 5.05 (dd, 1, 3′-H), 4.42 (m, 1, 4′-H), 4.17 (m, 2, 5′-H), 1.87 (s, 3, Ac), 1.55, 1.35 (s, 3+3, CMe_2); $J_{1',2'}=2$ Hz, $J_{2',3'}=6.4$ Hz, $J_{3',4'}=3.4$ Hz; CD (H_2O): $[\theta]_{286}$ −1600, $[\theta]_{268}$ −5300, $[\theta]_{243}$ −1600, $[\theta]_{231}$ −7500, $[\theta]_{221}$ 0, $[\theta]_{214}$ +4800, $[\theta]_{205}$ 0; (0.1 N HCl): $[\theta]_{293}$ −460, $[\theta]_{281}$ 0, $[\theta]_{271}$ +920, $[\theta]_{261}$ 0, $[\theta]_{228}$ −11300.

Reaction of 6 with NaCN——To a solution of **6** (0.84 g, 2 mmol) in DMF was added NaCN (0.25 g, 5.1 mmol) and the solution was stirred for 3 hr at room temperature. After the solution was neutralized with 1 N HCl it was partitioned with AcOEt and H_2O. The organic layer was dried over Na_2SO_4 and evaporated to dryness. The residue was taken in $CHCl_3$ and applied to a column of silica gel (2.5 × 12 cm). The eluate with 2% EtOH in $CHCl_3$ afforded 2′,3′,5′-tri-O-acetyl-N^6-acetyl-8-cyanoadenosine (56 mg, 5%) as a glass. UV $\lambda_{max}^{H_2O}$ 290 nm, λ_{min} 243 nm: MS *m/e*: 460 (M^+); IR (KBr): 2250 cm^{-1} (CN); NMR ($CDCl_3$), δ: 8.78 (s, 1, 2-H), 6.21 (m, 2, 1′,2′-H), 5.78 (m, 1, 3′-H), 4.45 (m, 3, 4′,5′-H), 2.66 (s, 3, NAc), 2.18, 2.09, 2.08 (s, 3+3+3, Ac_3). The eluate with 5% EtOH in $CHCl_3$ gave 2′,3′,5′-tri-O-acetyl-8-cyanoadenosine (**8**, 383 mg, 46%). UV $\lambda_{max}^{H_2O}$ 297 nm, λ_{min} 243 nm, $\lambda_{max}^{1N\ HCl}$ 277 nm, λ_{min}240 nm; MS *m/e*: 418 (M^+); IR (KBr): 2250 cm^{-1} (CN); NMR ($CDCl_3$), δ: 8.44 (s, 1, 2-H), 6.20 (m, 2, 1′,2′-H), 5.80 (m, 1, 3′-H), 4.45 (m, 3, 4′,5′-H), 2.17, 2.10, 2.07 (s, 3+3+3, Ac_3). The eluate with 8% EtOH in $CHCl_3$ gave the diacetate (87 mg, 12%), MS *m/e*: 376 (M^+); IR (KBr): 2250 cm^{-1} (CN).

Methyl Adenosine-8-carboximidate (9)——A solution of **8** (836 mg, 2 mmol) in abs. MeOH (30 ml) was added NaOMe (19 mg) and stirred at room temperature overnight. The precipitate was collected and washed with MeOH. This solid was crystallized from MeOH to give 437 mg (68%) of **9**, mp 206—207°. *Anal.* Calcd. for $C_{12}H_{16}N_6O_5$: C, 44.44; H, 4.97; N, 20.95. Found: C, 44.54; H, 5.02; N, 20.68. UV $\lambda_{max}^{H_2O}$ nm (ε): 284 (10600), 278 (sh, 10000), 223 (16400), λ_{min} 244 (3400); CD (H_2O): $[\theta]_{288}$ −1600, $[\theta]_{277}$ 0, $[\theta]_{260}$ +4100, $[\theta]_{250}$ +3100, $[\theta]_{230}$ +11300, $[\theta]_{223}$ 0, $[\theta]_{215}$ −7400, $[\theta]_{202}$ 0 (see Fig. 2); NMR: see Table I.

Methyl Adenosine-8-carboxylate (10)——To a solution of **9** (280 mg, 0.88 mmol) in MeOH (4 ml) and H_2O (10 ml) 1 N HCl (1 ml) was added and the solution was stirred for 2 hr at 0°. The solution was neutralized with Dowex 1 (bicarbonate) resin and the filtrate was concentrated to leave crystalline material.

This was washed with acetone to give 236 mg (88%) of **10**, mp 199—200°. *Anal.* Calcd. for $C_{12}H_{15}N_5O_6 \cdot 1/2H_2O$: C, 43.10; H, 4.83; N, 20.95. Found: C, 42.83; H, 4.80; N, 20.83. UV $\lambda_{\max}^{H_2O}$ nm (ε): 298 (11600), 227 (17000), $\lambda_{\min}$ 246 (2900), $\lambda_{\max}^{0.5\,N\ HCl}$ 279 (14800), 244 (4100); IR (KBr): 1740 cm^{-1}; CD (H_2O): $[\theta]_{299}$ -1200, $[\theta]_{283}$0, $[\theta]_{257}$$+4000$, $[\theta]_{226}$ 0, $[\theta]_{218}$ -2200 (see Fig. 2); NMR: see Table I.

Sodium Salt of Adenosine-8-carboxylic Acid (11)——A solution of **10** (141 mg, 0.42 mmol) in 0.1 N NaOH (5.5 ml) was stirred for 30 min at room temperature. The solution was neutralized with 1 N HCl to pH 4 and the precipitated material was collected to furnish 104 mg of the free acid, mp 140—155°. This powder contained a small amount of adenosine. The free acid was neutralized with 1 N NaOH and crystallized from MeOH–H_2O to give **11**, mp>300°. *Anal.* Calcd. for $C_{11}H_{12}N_5O_6Na \cdot H_2O$: C, 37.59; H, 4.03; N, 19.94. Found: C, 37.70; H, 3.72; N, 19.47. UV $\lambda_{\max}^{H_2O}$ nm (ε): 275 (10800), $\lambda_{\min}$ 242 (3500), $\lambda_{\max}^{0.05N\ HCl}$ 275 (13100), $\lambda_{\min}$ 241 (3800); CD (H_2O): $[\theta]_{260}$ $+5000$, $[\theta]_{250}$ $+4500$, $[\theta]_{233}$ $+11800$, $[\theta]_{220}$ 0, $[\theta]_{212}$ -2100; NMR: see Table I.

2′,3′-O-Isopropylideneadenosine-8-carboxamide (12)——A mixture of **7** (500 mg, 1.3 mmol) in tetrahydrofurane (5 ml) and 1 N NaOH (5 ml) was stirred at room temperature for one hr. The solution was neutralized with Dowex 50 (H^+) resin. After removal of the resin the filtrate was concentrated and the residue was crystallized from H_2O to give 450 mg (94%) of **12**, mp 156—157°. *Anal.* Calcd. for $C_{14}H_{18}N_6O_5 \cdot H_2O$: C, 45.64; H, 5.48; N, 22.82. Found: C, 45.66; H, 5.31; N, 22.77. UV $\lambda_{\max}^{H_2O}$ nm (ε): 291 (10700), $\lambda_{\min}$ 245 (2550), $\lambda_{\max}^{0.5N\ HCl}$ 275 (14150), $\lambda_{\min}$ 241 (4100), $\lambda_{\max}^{0.5N\ NaOH}$ 291 (10250), $\lambda_{\min}$ 245 (3550); MS *m/e*: 350 (M^+); IR (KBr): 1700 cm^{-1}; NMR (DMSO-d_6), δ: 8.21 (s, 1, 2-H), 8.03 (bs, 2, $CONH_2$), 7.59 (bs, 2, NH_2), 7.07 (s, 1, 1′-H), 5.48 (dd, 1, 2′-H), 5.03 (dd, 1, 3′-H), 4.09 (m, 1, 4′-H), 3.37 (m, 2, 5′-H), 1.54, 1.31 (s, 3+3, CMe_2); $J_{1',2'}$= 2.9 Hz, $J_{2',3'}$=6.2 Hz, $J_{3',4'}$=3.7 Hz; CD (H_2O): $[\theta]_{295}$ -1000, $[\theta]_{286}$ 0, $[\theta]_{266}$ $+6000$, $[\theta]_{248}$ $+3600$, $[\theta]_{240}$ $+3900$, $[\theta]_{223}$ -10200, $[\theta]_{214}$ 0, $[\theta]_{210}$ $+6700$, $[\theta]_{206}$ 0, $[\theta]_{200}$ -8300; (0.1 N HCl): $[\theta]_{320}$ -200, $[\theta]_{310}$ 0, $[\theta]_{273}$ $+6900$, $[\theta]_{252}$ 0, $[\theta]_{232}$ $+9000$, $[\theta]_{220}$ -3200, $[\theta]_{213}$ -3500.

Adenosine-8-carboxamide (13)——A suspension of **8** (209 mg, 0.5 mmol) in H_2O (5 ml) and 1 N NaOH (2 ml) was stirred at room temperature for 2 hr and the resulting solution was neutralized with Dowex 50 (H^+) resin. After the resin was removed, the filtrate was evaporated to dryness. The residue was crystallized from H_2O to give 78 mg (50%) of **13**, mp 249—251°. *Anal.* Calcd. for $C_{11}H_{14}N_6O_5 \cdot 1/2H_2O$: C, 41.38;H, 4.41; N, 26.32. Found: C, 41.69; H, 4.53; N, 26.41. UV $\lambda_{\max}^{H_2O}$ nm (ε): 287 (10700), 222 (18300), $\lambda_{\min}$ 243 (3700), $\lambda_{\max}^{0.1N\ HCl}$ 274 (14000), $\lambda_{\min}$ 241 (4800), $\lambda_{\max}^{0.1N\ NaOH}$ 281 (10500), $\lambda_{\min}$ 243 (4400); CD (H_2O): $[\theta]_{261}$ $+7700$, $[\theta]_{228}$ 0, $[\theta]_{222}$ -6800, $[\theta]_{217}$ 0, $[\theta]_{209}$ $+5400$, $[\theta]_{204}$ 0; (0.1 N HCl): $[\theta]_{265}$ $+7800$, $[\theta]_{242}$ 0, $[\theta]_{233}$ -4100, $[\theta]_{224}$ 0, $[\theta]_{220}$ $+1400$, $[\theta]_{218}$ 0, $[\theta]_{210}$ -7400, $[\theta]_{200}$ -3700 (see Fig. 2); NMR: see Table I.

2′,3′-O-Isopropylidene-5′-O-acetyladenosine-8-thiocarboxamide (14)——To a solution of **7** (1.0 g, 2.7 mmol) in 10 ml of pyridine was bubbled H_2S at 0° for 2 hr under stirring. The mixture was evaporated to dryness to leave a crystalline material which was recrystallized from MeOH–hexane to give 0.77 g (70%) of **14**, mp 113—114°. *Anal.* Calcd. for $C_{16}H_{20}N_6O_5S$: C, 47.04; H, 4.95; N, 20.58; S, 7.85. Found: C, 46.87; H, 4.95; N, 20.37; S, 7.83. UV $\lambda_{\max}^{H_2O}$ nm (ε): 308 (sh, 10800), 276 (11600), 263 (11000), 218 (16800), $\lambda_{\min}$ 242 (7200), $\lambda_{\max}^{1N\ HCl}$ 285 (sh, 11800), 268 (16400), $\lambda_{\min}$ 235 (9400), $\lambda_{\max}^{1N\ NaOH}$ 260 (18200), $\lambda_{\min}$ 235 (9400); MS *m/e*: 408: M^+; NMR (DMSO-d_6), δ: 10.55, 10.18 (bs, 1+1, $CSNH_2$), 8.21 (s, 1, 2-H), 7.54 (bs, 2, NH_2), 7.00 (s, 1, 1′-H), 5.57 (dd, 1, 2′-H), 5.14 (dd, 1, 3′-H), 4.19 (m, 3, 4′,5′-H), 1.96 (s, 3, Ac), 1.52, 1.33 (s, 3+3, CMe_2); $J_{1',2'}$= 1.9 Hz, $J_{2',3'}$=6.2 Hz, $J_{3',4'}$=2.9 Hz.

2′,3′-O-Isopropylideneadenosine-8-thiocarboxamide (15)——A mixture of **14** (204 mg, 0.5 mmol) and NaOMe (16 mg, 0.25 mmol) in abs. MeOH (10 ml) was stirred at room temperature for 24 hr, and neutralized with Dowex 50 (H^+) resin. After removal of the resin the filtrate was evaporated to dryness. The residue was crystallized from EtOH–H_2O to give 120 mg (66%) of **15**, mp 175—177°. *Anal.* Calcd. for $C_{14}H_{18}N_6O_4S$: C, 45.88; H, 4.96; N, 22.94; S, 8.75. Found: C, 45.98; H, 4.96; N, 22.94; S, 8.60. UV $\lambda_{\max}^{H_2O}$ nm (ε): 308 (sh, 10800), 276 (11600), 263 (sh, 11100), 218 (16800), $\lambda_{\min}$ 242 (7200), 207 (16400); MS *m/e*: 366 (M^+); NMR (DMSO-d_6), δ: 10.55, 10.09 (bs, 1+1, $CSNH_2$), 8.19 (s, 1, 2-H), 7.59 (bs, 2, NH_2), 6.86 (d, 1, 1′-H), 5.54 (dd, 1, 2′-H), 5.21 (t, 1, 5′-OH), 5.00 (dd, 1, 3′-H), 4.11 (m, 1, 4′-H), 3.50 (m, 2, 5′-H), 1.52, 1.32 (s, 3+3, CMe_2); $J_{1',2'}$=2.9 Hz, $J_{2',3'}$=6.0 Hz, $J_{3',4'}$=2.9 Hz; CD (H_2O): $[\theta]_{385}$ $+3800$, $[\theta]_{350}$ 0, $[\theta]_{325}$ -4700, $[\theta]_{300}$ 0, $[\theta]_{282}$ $+2600$, $[\theta]_{270}$ 0, $[\theta]_{241}$ -11500, $[\theta]_{216}$ 0, $[\theta]_{200}$ -5900.

2′,3′,5′-Tri-O-acetyladenosine-8-thiocarboxamide (16)——To a solution of **8** (670 mg, 1.6 mmol) in 10 ml of pyridine H_2S was bubbled at 0° for one hr and the stoppered solution was kept at room temperature for 4 days. The solution was concentrated to dryness to leave a yellow residue. This was crystallized from MeOH–H_2O to give 526 mg (75%) of **16**, mp 191—192°. *Anal.* Calcd. for $C_{17}H_{20}N_6O_7S$: C, 45.12; H, 4.46; N, 18.58; S, 7.09. Found: C, 45.09; H, 4.48; N, 18.51; S, 6.83. MS *m/e*: 452 (M^+); NMR (DMSO-d_6), δ: 8.22 (s, 1, 2-H), 7.58 (bs, 2, NH_2), 6.84 (d, 1, 1′-H), 6.25 (dd, 1, 2′-H), 5.75 (m, 1, 3′-H), 4.32 (m, 3, 4′,5′-H), 2.09, 2.04, 1.97 (s, 3+3+3, Ac_3); $J_{1.'2'}$=4.4 Hz, $J_{2',3'}$=6.2 Hz; CD (H_2O): $[\theta]_{385}$ $+4200$, $[\theta]_{345}$ 0, $[\theta]_{315}$ -6600, $[\theta]_{285}$ 0, $[\theta]_{275}$ $+1400$, $[\theta]_{263}$ 0, $[\theta]_{243}$ -4800, $[\theta]_{235}$ 0, $[\theta]_{225}$ $+8900$, $[\theta]_{216}$ 0, $[\theta]_{200}$ -14700; (0.1 N HCl): $[\theta]_{385}$ $+3600$, $[\theta]_{331}$ 0, $[\theta]_{305}$ -3600, $[\theta]_{286}$ 0, $[\theta]_{272}$ $+3000$, $[\theta]_{261}$ 0, $[\theta]_{245}$ -11000, $[\theta]_{230}$ 0, $[\theta]_{222}$ $+8400$, $[\theta]_{212}$ 0, $[\theta]_{204}$ -11400.

Adenosine-8-thiocarboxamide (17)——A solution of **16** (269 mg, 0.82 mmol) and NaOMe (22 mg) in 20 ml of MeOH was stirred for 2 hr at room temperature. After neutralization of the solution with Dowex 50 (H^+), and removal of the resin, the solution was evaporated and the residue was crystallized from H_2O to give 130 mg (49%) of **17**, mp 179—180°. *Anal.* Calcd. for $C_{11}H_{14}N_6O_4S$: C, 40.49; H, 4.32; N, 25.75; S, 9.82. Found: C, 40.58; H, 4.39; N, 25.59; S, 9.68. UV $\lambda_{max}^{H_2O}$ nm (ε): 281 (102000), 227 (14200), λ_{min} 250 (6500), $\lambda_{max}^{0.1N\ HCl}$ 275 (15200, λ_{min} 245 (7200), $\lambda_{max}^{0.1N\ NaOH}$ 268 (17000), λ_{min} 243 (8900); CD (H_2O): $[\theta]_{381}$ +8500, $[\theta]_{347}$ 0, $[\theta]_{315}$ −14900, $[\theta]_{292}$ 0, $[\theta]_{276}$ +13600, $[\theta]_{262}$ 0, $[\theta]_{245}$ −18200, $[\theta]_{237}$ 0, $[\theta]_{230}$ +18000, $[\theta]_{223}$ 0, $[\theta]_{215}$ −15700, $[\theta]_{200}$ 0. NMR: see Table I.

2′,3′,5′-Tri-O-acetyl-2-methylthioadenosine (18)——A mixture of 2-methylthioadenosine17) (238 mg, 0.76 mmol) and acetic anhydride (1 ml) in pyridine (10 ml) was kept at room temperature for 1.5 hr. The solution was added H_2O and was evaporated. The evaporation with H_2O was repeated and the final residue was crystallized from EtOH–H_2O to give 281 mg (84%) of **18**, mp 185—186°. *Anal.* Calcd. for $C_{17}H_{21}N_5O_7S$: C, 46.44; H, 4.83; N, 15.94; S, 7.29. Found: C, 46.28; H, 4.76; N, 15.84; S, 7.35. UV $\lambda_{max}^{H_2O}$ nm (ε): 274 (14300), 235.5 (21150), λ_{min} 251 (8400), 217 (10300), $\lambda_{max}^{1N\ HCl}$ 282 (sh, 13000), 270.5 (16300), 220 (16400), λ_{min} 242 (4750); MS *m/e*: 439 (M^+); NMR (DMSO-d_6), δ: 7.78 (s, 1, 8-H), 6.05 (bs, 4, NH_2, 1′,2′-H), 5.74 (m, 1, 3′-H), 4.42 (bs, 3, 4′,5′-H), 2.57 (s, 3, SMe), 2.14, 2.11, 2.06 (s, 3+3+3, Ac_3); CD (H_2O): $[\theta]_{280}$ +1360, $[\theta]_{260}$ 0, $[\theta]_{249}$ −1020, $[\theta]_{244}$ 0, $[\theta]_{227}$ +6800, $[\theta]_{217}$ +2560, $[\theta]_{210}$ +5800, $[\theta]_{204}$ 0, $[\theta]_{202}$ −12600.

2′,3′,5′-Tri-O-acetyl-2-methylsulfonyladenosine (19)——To a solution of **18** (222 mg, 0.5 mmol) in 10 ml of 50% acetic acid $KMnO_4$ (200 mg) was added in an ice-bath under stirring. After one hr 35% H_2O_2 solution was added until the solution became colorless. The solution was extracted with $CHCl_3$ and the organic layer was dried over Na_2SO_4, and evaporated. The residue was crystallized from EtOH to give 212 mg (89%) of **19**, mp 138—139°. *Anal.* Calcd. for $C_{17}H_{21}N_5O_9S$: C, 43.29; H, 4.50; N, 14.86; S, 6.79. Found: C, 43.41; H, 4.47; N, 14.73; S, 6.62. UV $\lambda_{max}^{H_2O}$ nm (ε): 280 (sh, 6800), 263 (12300), λ_{min} 236 (3100), $\lambda_{max}^{0.5N\ HCl}$ 278 (sh, 7500), 262.5 (12000), λ_{min} 236 (3100); MS *m/e*: 471 (M^+); NMR (DMSO-d_6), δ: 8.16 (s, 1, 8-H), 7.04 (bs, 2, NH_2), 6.19 (d, 1, 1′-H), 5.96 (dd, 1, 2′-H), 5.68 (dd, 1, 3′-H), 4.41 (bs, 3, 4′,5′-H), 3.35 (s, 3, SO_2Me), 2.15, 2.12, 2.07 (s, 3+3+3, Ac_3); $J_{1',2'}=4.4$ Hz; CD (H_2O): $[\theta]_{276}$ −2400, $[\theta]_{244}$ 0, $[\theta]_{225}$ −4900, $[\theta]_{222}$ 0, $[\theta]_{212}$ +9570, $[\theta]_{202}$ 0.

Reaction of 19 with NaCN——A mixture of **19** (4.71 g, 10 mmol) and NaCN (735 mg, 15 mmol) in 30 ml of DMF was stirred for one hr at room temperature. The mixture was evaporated to leave a residue which was partitioned with $CHCl_3$ and H_2O. The organic layer was dried and evaporated to dryness. The resulted glass was dissolved in $CHCl_3$ and applied to a column of silica gel (2.8×30 cm). The initial eluate with 2% EtOH in $CHCl_3$ was evaporated to give 318 mg (6.9%) of the tetra-acetate as a glass, UV $\lambda_{max}^{H_2O}$ 278 and 232 nm, λ_{min} 248 and 216 nm; MS *m/e*: 460 (M^+); IR (direct): 2250 cm^{-1} (CN); NMR (DMSO-d_6), δ: 11.25 (s, 1, 6-NH), 8.93 (s, 1, 8-H), 6.35 (d, 1, 1′-H), 5.96 (dd, 1, 2′-H), 5.65 (dd, 1, 3′-H), 4.38 (bs, 3, 4′,5′-H), 2.29, 2.13, 2.06, 2.03 (s, Ac_4). The latter portion of the eluate with 2% EtOH in $CHCl_3$ was evaporated and the residue was crystallized from MeOH–H_2O to give 2.81 g (67%) of **20**, mp 114—116°. *Anal.* Calcd. for $C_{17}H_{18}N_6O_7\cdot 1/2H_2O$: C, 47.75; H, 4.49; N, 19.66. Found: C, 47.88; H, 4.41; N, 19.42. UV $\lambda_{max}^{H_2O}$ nm (ε): 298 (6500), 266.5 (10400), 264 (sh, 9970), λ_{min} 276 (4480), 241 (2650), $\lambda_{max}^{0.5N\ HCl}$ 296 (6600), 266.5 (10400), 264 (sh, 9980), λ_{min} 277 (5350), 241 (3800); MS *m/e*: 418 (M^+); IR (nujol): 2260 cm^{-1}; NMR (DMSO-d_6), δ: 8.12 (s, 1, 8-H), 6.18 (d, 1, 1′-H), 6.00 (bs, 2, NH_2), 5.78 (dd, 1, 2′-H), 5.77 (dd, 1, 3′-H), 4.43 (bs, 3, 4′,5′-H), 2.17, 2.15, 2.09 (s, 3+3+3, Ac_3); $J_{1',2'}=5.4$ Hz; CD (H_2O): $[\theta]_{290}$ −1700, $[\theta]_{275}$ −1500, $[\theta]_{266}$ −1700, $[\theta]_{250}$ 0, $[\theta]_{231}$ −4800, $[\theta]_{225}$ 0, $[\theta]_{215}$ +9300. The eluate with 16% EtOH in $CHCl_3$ was evaporated to give the diacetate (615 mg, 16%, as a glass), UV $\lambda_{max}^{H_2O}$ 296, 267, 263 sh nm; MS *m/e*: 376 (M^+); IR (direct): 2260 cm^{-1} (CN).

Methyl Adenosine-2-carboximidate (21)——A mixture of **20** (418 mg, 1 mmol) and NaOMe (30 mg) in 30 ml of MeOH was stirred for 17 hr at room temperature. After neutralization of the solution with Dowex 50 (H^+) resin and filtration of the resin, the filtrate was concentrated. The residue was crystallized from MeOH–acetone to give 288 mg (88.9%) of **21**, mp 169—170°. *Anal.* Calcd. for $C_{12}H_{16}N_6O_5$: C, 44.42; H, 4.99; N, 25.91. Found: C, 44.54; H, 5.02; N, 25.70. UV $\lambda_{max}^{H_2O}$ nm (ε): 293 (5800), 266.5 (10700), 263 (sh, 10500), λ_{min} 277 (5000), 244 (5300); CD (H_2O): $[\theta]_{292}$ −1900, $[\theta]_{261}$ 0, $[\theta]_{234}$ −8200, $[\theta]_{226}$ 0, $[\theta]_{217}$ +9400 (see Fig. 1); NMR see Table I.

Methyl Adenosine-2-carboxylate (22)——A solution of **21** (288 mg, 0.89 mmol) in MeOH (15 ml), H_2O (10 ml), and 1 N HCl (1 ml) was stirred at room temperature for 2 hr. After neutralization of the solution with Dowex 1 (bicarbonate) and filtration of the resin, the solution was evaporated and the residue was crystallized from MeOH–H_2O to give 255 mg (88%) of **22**, mp 135—137°. *Anal.* Calcd. for $C_{12}H_{15}N_5O_6$: C, 44.31; H, 4.65; N, 21.53. Found: C, 43.80; H, 4.52; N, 21.55. UV $\lambda_{max}^{H_2O}$ nm (ε): 296 (6000), 264 (10000), 260 (sh, 9800), λ_{min} 274 (4400), 242 (5000); CD (H_2O): $[\theta]_{293}$ −1500, $[\theta]_{256}$ 0, $[\theta]_{233}$ −7700, $[\theta]_{224}$ 0, $[\theta]_{214}$ +9700 (see Fig. 1); NMR: see Table I.

Sodium Salt of Adenosine-2-carboxylic Acid (23)——A suspension of **22** (163 mg, 0.5 mmol) in 2 ml of H_2O and 0.52 ml of 1 N NaOH was stirred at room temperature for 2 hr. The homogeneous solution was concentrated to a half volume and MeOH was added to a slight turbidity. The separated crystals were collected to give a hydroscopic **23** (134 mg, 80%), mp>300°. *Anal.* Calcd. for $C_{11}H_{12}N_5O_6Na\cdot 1/2H_2O$: C, 38.57; H, 3.84; N, 20.47. Found: C, 38.27; H, 3.93; N, 20.25. IR (KBr): 1640 cm^{-1}; CD (H_2O): $[\theta]_{268}$ −2450, $[\theta]_{243}$ −250, $[\theta]_{226}$ −2200, $[\theta]_{220}$ 0. NMR: see Table I.

Adenosine-2-carboxamide (24)——A suspension of **20** (1.67 g, 4 mmol) in H_2O (50 ml) and 1 N NaOH (12 ml) was stirred for 4 days at room temperature. The solution was neutralized with Dowex 50 (H^+) resin, the resin was removed by filtration, and the filtrate was concentrated. The residue was crystallized from H_2O to give 570 mg (46%) of **24**, mp 145—147°. *Anal.* Calcd. for $C_{11}H_{14}N_6O_5$: C, 42.58; H, 4.55; N, 27.09. Found: C, 42.62; H, 4.53; N, 26.95. UV $\lambda_{\max}^{H_2O}$ nm (ε): 291 (6800), 266 (11700), 263 (sh, 11400), $\lambda_{\min}$ 276 (5900), 243.5 (5600), $\lambda_{\max}^{0.5N\ HCl}$ 283—290 (6400), 267 (13700), $\lambda_{\min}$ 243.5 (7400); CD (H_2O): $[\theta]_{280}$ -2000, $[\theta]_{255}$ -550, $[\theta]_{228}$ -6800, $[\theta]_{225}$ 0, $[\theta]_{217}$ $+5300$ (see Fig. 1); NMR: see Table I.

2′,3′,5′-Tri-O-acetyl-8-cyanoinosine (25)——To a solution of **8** (250 mg) in 90% acetic acid was added $NaNO_2$ (150 mg) in an ice-bath and the solution was stirred for 22 hr at room temperature. The solution was concentrated and the residue was partitioned with $CHCl_3$ and H_2O. The organic layer was dried (Na_2SO_4) and evaporated to dryness. The residue was crystallized from EtOH–hexane to give 58 mg of **25**, mp 92—95°. *Anal.* Calcd. for $C_{17}H_{17}N_5O_8$: C, 48.69; H, 4.09; N, 16.69. Found: C, 48.46; H, 3.99; N, 16.62. UV $\lambda_{\max}^{H_2O}$ 283.5 nm, $\lambda_{\min}$ 241 nm, $\lambda_{\max}^{0.1N\ NaOH}$ 301 nm, $\lambda_{\min}$ 245 nm; IR (KBr): 2250 cm^{-1} (CN); NMR (DMSO-d_6), δ: 12.91 (bs, 1, N^1–H), 8.32 (s, 1, 2-H), 6.22 (d, 1, 1′-H), 5.87 (dd, 1, 2′-H), 5.62 (dd, 1, 3′-H), 4.46 (m, 3, 4′,5′-H), 2.11, 2.07, 1.97 (s, 3+3+3, Ac_3), $J_{1',2'}=4.2$ Hz; MS *m/e*: 419 (M^+).

Inosine-2-carboxylic Acid (26)——To a solution of **20** (1.25 g, 3 mmol) in 50 ml of 90% acetic acid was added $NaNO_2$ (620 mg) in an ice-bath and the solutions was stirred at room temperature for 24 hr. Further addition of $NaNO_2$ (400 mg) to the solution and stirring for 24 hr resulted in a completion of the reaction. The mixture was concentrated to dryness and the residue was extracted with hot EtOH. The separated precipitate, on cooling the EtOH solution, was collected to give 1.2 g of sodium 2′,3′,5′-tri-O-acetylinosine-2-carboxylate, NMR (DMSO-d_6), δ: 8.20 (s, 1, 8-H), 6.11 (d, 1, 1′-H), 5.83 (t, 1, 2′-H), 5.57 (m, 1,3′-H), 4.31 (bs, 3, 4′,5′-H), 2.12, 2.04 (s, 3+6, Ac_3); $J_{1',2'}=5.6$ Hz. The product was dissolved in abs. MeOH (25 ml) containing 100 mg of NaOMe and the solution was stirred at room temperature for 24 hr. The solution was evaporated to dryness and the residue was dissolved in H_2O–EtOH. To the solution was added 1 N HCl to the little turbidity, and it was kept in a refrigerator. The separated crystals were collected (510 mg of **26**), mp>300°. UV $\lambda_{\max}^{H_2O}$ 284, 254, 247.5 nm, $\lambda_{\min}$ 264, 251, 233 nm; NMR (DMSO-d_6), δ: 12.50 (bs, 1, N^1–H), 8.48 (s, 1, 8-H), 5.91 (d, 1, 1′-H), 4.52 (t, 1, 2′-H), 4.15 (t, 1, 3′-H), 3.75 (m, 1, 4′-H), 3.61 (bs, 2, 5′-H); $J_{1',2'}=6.1$ Hz.