Title	Variation in the suger moiety of 5-amino-4-imidazolecarboxamide riboside
Sub Title	
Author	柳沢, 宏明(Yanagisawa, Hiroaki) 木下, 光博(Kinoshita, Mitsuhiro) 梅澤, 純夫(Umezawa, Sumio)
Publisher	慶応義塾大学工学部
Publication year	1971
Jtitle	Keio engineering reports Vol.24, No.1 (1971.) ,p.1- 7
JaLC DOI	
Abstract	The 4-cyano-5'-mesyl derivative (2) prepared from 2', 3'-0-isopropylidene-AICAR was allowed to react with various nucleophiles, sodium azide and potassium iodide. The reaction products were reduced and/or hydrated to afford 5'-amino-5'-deoxy- and 5'-deoxy-AICAR and their 4-cyano derivatives. Deacetylation of 5'-S-acetyl derivative from 2 with potassium thioacetate gave a disulfide.
Notes	
Genre	Departmental Bulletin Paper
URL	https://koara.lib.keio.ac.jp/xoonips/modules/xoonips/detail.php?koara_id=KO50001004-00240001-0001

KEIO ENGINEERING REPORTS
VOL. 24 NO. 1

VARIATION IN THE SUGAR MOIETY 5-AMINO-4-IMIDAZOLECARBOXAMIDE RIBOSIDE

BY

HIROAKI YANAGISAWA, MITSUHIRO KINOSHITA
and *SUMIO UMEZAWA*

FACULTY OF ENGINEERING
KEIO UNIVERSITY
TOKYO 1971

VARIATION IN THE SUGAR MOIETY OF 5-AMINO-4-IMIDAZOLECARBOXAMIDE RIBOSIDE

HIROAKI YANAGISAWA, MITSUHIRO KINOSHITA, AND SUMIO UMEZAWA

Dept. of Applied Chemistry, Keio University, Koganei-shi, Tokyo 184

(Received June 2, 1971)

ABSTRACT

The 4-cyano-5′-mesyl derivative (**2**) prepared from 2′,3′-*O*-isopropylidene-AICAR was allowed to react with various nucleophiles, sodium azide and potassium iodide. The reaction products were reduced and/or hydrated to afford 5′-amino-5′-deoxy- and 5′-deoxy-AICAR and their 4-cyano derivatives. Deacetylation of 5′-S-acetyl derivative from **2** with potassium thioacetate gave a disulfide.

5-Amino-4-imidazolecarboxamide riboside (AICAR) (GREENBERG and SPILMAN, 1956; SHIRO, YAMANOI, et al. 1962) is an important intermediate in the biosynthesis of purine nucleotides and is at present industrially produced, being used as a starting material for the syntheses (YAMAZAKI, KUMASHIRO, et al. 1967) of 5′-guanylic acid (a flavor-enhancing agent). Recently, the modifications of the base moiety in AICAR have been studied (YAMAZAKI, KUMASHIRO, et al. 1968; MONTGOMERY and THOMAS, 1969) and it has been known that some variants have antitumor activity (HAYASHI, KUMAGAI, et al. 1968), however, little is known about the variation of the sugar moiety of AICAR. This paper described the replacement of 5′-hydroxyl group in the ribose moiety with azido-, amino-, and thiol-group and iodine and hydrogen through 5′-*O*-mesyl derivative.

Treatment of 5-amino-4-carbamoyl-1-(2′,3′-*O*-isopropylidene-β-D-ribofuranosyl)-imidazole (**1**)* derived from AICAR with 2.1 equivalent moles of methanesulfonyl chloride in pyridine gave 5-amino-4-cyano-1-(2′,3′-*O*-isopropylidene-5′-*O*-methanesulfonyl-β-D-ribofuranosyl) imidazole (**2**). The dehydration of 4-carbamoyl group in the imidazole ring to cyano group was shown by the elemental analysis, IR spectrum ($\nu_{C\equiv N}$ 2220 cm^{-1}) and UV spectrum (λ_{max}^{MeOH} 246 mμ).

---

* We modified the method in Neth. Appl. 6,409,142 (Ajinomoto Co., Inc.): Preparation of 5-Amino-4-carbamoyl-1-(2′,3′-*O*-isopropylidene-β-D-ribofuranosyl) imidazole. *CA.*, **63**, 5731b (1965).

Treatment of **2** with sodium azide as a nucleophile afforded 5-amino-1-(5′-azido-5′-deoxy-2′, 3′-*O*-isopropylidene-β-D-ribofuranosyl)-4-cyanoimidazole (**3**). The hydration of **3** with hydrogen peroxide-ammonium hydroxide (WIBERG, 1953) afforded 5-amino-1-(5′-azido-5′-deoxy-2′, 3′-*O*-isopropylidene-β-D-ribofuranosyl)-4-carbamoylimidazole (**4**), which was then hydrogenated with palladium black to afford 5-amino-1-(5′-amino-5′-deoxy-2′, 3′-*O*-isopropylidene-β-D-ribofuranosyl)-4-carbamoylimidazole (**5**). The 2′, 3′-*O*-isopropylidene group in **5** was removed with 30% acetic acid to afford 5-amino-1-(5′-amino-5′-deoxy-β-D-ribofuranosyl)-4-carbamoylimidazole (**6**).

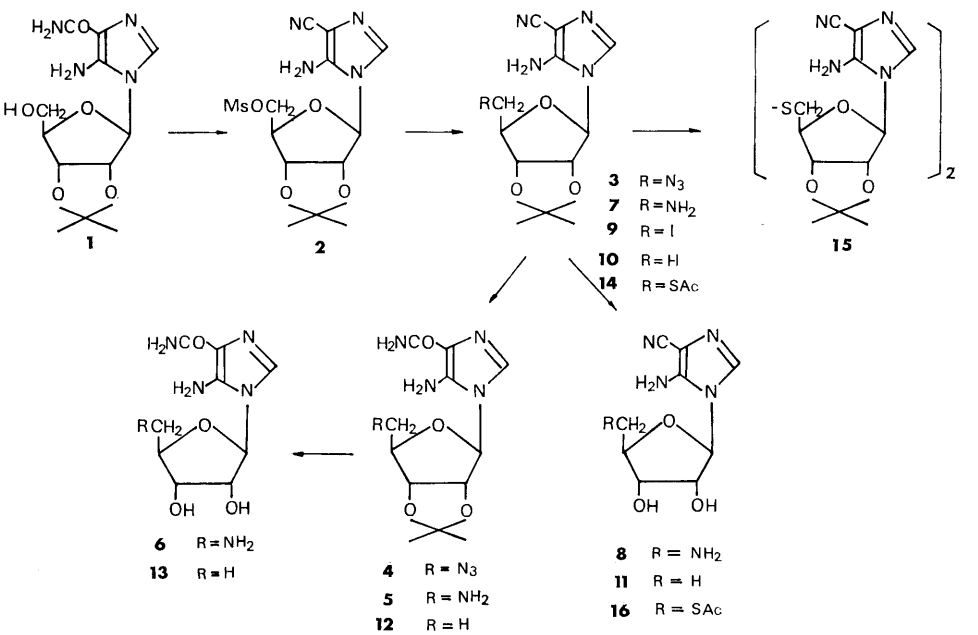

Fig. 1.

Hydrogenation of **3** with palladium black afforded 5-amino-1-(5′-amino-5′-deoxy-2′, 3′-*O*-isopropylidene-β-D-ribofuranosyl)-4-cyanoimidazole (**7**). It is noteworthy that the 4-cyano group of **3** was not reduced in this hydrogenation. Removal of the isopropylidene group of **7** with 30% acetic acid afforded 4-amino-1-(5′-amino-5′-deoxy-β-D-ribofuranosyl)-4-cyanoimidazole (**8**).

Reaction of **2** with potassium iodide afforded 5-amino-4-cyano-1-(5′-deoxy-5′-iodo-2′, 3′-*O*-isopropylidene-β-D-ribofuranosyl) imidazole (**9**). The iodide (**9**) was reduced with palladium black to give 5-amino-4-cyano-1-(5′-deoxy-2′, 3′-*O*-isopropylidene-β-D-ribofuranosyl) imidazole (**10**), which was then hydrolyzed with 30% acetic acid to afford 5-amino-4-cyano-1-(5′-deoxy-β-D-ribofuranosyl) imidazole (**11**).

Conversion of the 4-cyano group of **10** to carbamoyl group was effected with hydrogen peroxide-ammonium hydroxide to afford 5-amino-4-carbamoyl-1-(5′-deoxy-2′, 3′-*O*-isopropylidene-β-D-ribofuranosyl) imdazole (**12**). Removal of the isopropylidene group in **12** with 30% acetic acid afforded 5-amino-4-carbamoyl-1-(5′-deoxy-β-D-ribofuranosyl) imidazole (**13**).

Finally, **2** was allowed to react with potassium thioacetate to give 5-amino-1-(5′-acetylthio-5′-deoxy-2′, 3′-*O*-isopropylidene-β-D-ribofuranosyl)-4-cyanoimidazole (**14**). In this case, the hydration of 4-cyano group with hydrogen peroxide-ammonium hydroxide was unsuccessful and a disulfide, namely 5′ 5′-dithiobis [5-amino-4-cyano-1-(5′-deoxy-2′, 3′-*O*-isopropylidene-β-D-ribofuranosyl) imidazole] (**15**) was obtained. The disulfide bond was confirmed by triphenyltetrazolium test on thin layer chromatography where **15** was negative but **14** was positive. Removal of the isopropylidene group of **14** with 30% acetic acid afforded 5-amino-1-(5′-acetylthio-5′-deoxy-β-D-ribofuranosyl)-4-cyanoimidazole (**16**).

Biological tests for the above-mentioned compounds (**6**, **8**, **11**, **13** and **16**) are in progress.

EXPERIMENTAL

Melting point determinations were carried out on a micro hot stage and were uncorrected. Thin layer chromatography (TLC) was conducted by the use of silica gel (Daiichi Pure Chemicals Co., Inc.). Silica gel column chromatography carried out with WAKOGEL C-200 (Wako Pure Chemical Industries, Ltd.). NMR spectra were taken with a Varian A-60D spectrometer. UV spectra were recorded on a Hitachi Perkin-Elmer UV-VIS spectrometer 139. IR spectra were taken in a Hitachi IPI-2 spectrometer. Optical rotations were measured with a Zeiss Photoelectric Polarimeter.

5-*Amino*-4-*carbamoyl*-1-(2′, 3′-O-*isopropylidene*-β-D-*ribofuranosyl*)-*imidazole* (**1**). To an ice-cooling suspension of AICAR (2.00 g), 2, 2-dimethoxypropane (10 m*l*) and Drierite (8.0 g) in absolute methanol (32 m*l*) and absolute acetone (32 m*l*) was added concentrated sulfuric acid (0.6 m*l*) with stirring, and the stirring was continued for 15 hr at room temperature. The reaction mixture was neutralized with Amberlite IRA-400 (OH type). The resin and precipitates were removed by filtration and washed with ethanol. The filtrate and washings were combined and evaporated to dryness. The isopropylidene derivative (**1**) was obtained as a pale yellow glass, yield 1.79 g (78.0%).

5-*Amino*-4-*cyano*-1-(2′, 3′-O-*isopropylidene*-5′-O-*methanesulfonyl*-β-D-*ribofuranosyl*) *imidazole* (**2**). Methanesulfonyl chloride (1.85 m*l*) was added to an ice-cooled solution of 5-amino-4-carbamoyl-1-(2′, 3′-*O*-isopropylidene-β-D-ribofuranosyl) imidazole (**1**) (3.28 g) in pyridine (20 m*l*) under stirring. After stirring for 2 hr under ice-cooling, the mixture was poured into ice-water (150 m*l*) and then stirred for 1 hr. The precipitates were collected by filtration and washed with water to give colorless crystals of **2**, yield 2.58 g (65.7%). An analytical smple was obtained by recrystallization from ethyl acetate-diisopropyl ether: mp 179-181°C; $[\alpha]_D^{23}$ -85° (c 1.6, methanol); ν_{max}^{nujol} 2220, 1740, 1651, 1507, 1172, and 1156 cm^{-1}; λ_{max}^{MeOH} 246 mμ (ε 13450); $\tau(C_5D_5N)$ 2.18

(s, H-2), 3.82 (d, H-1′, $J_{1',2'}$=3.1 Hz), 4.56 (d, d, H-2′, $J_{2',3'}$=6.7 Hz), 4.82 (d, d, H-3′, $J_{3',4'}$=3.0 Hz), 6.76 (s, OSO_2CH_3), 8.47, and 8.65 (s, $=C(CH_3)_2$).

Found: C, 44.00; H, 5.68; N, 15.46; S, 9.46%. Calcd for $C_{13}H_{18}N_4O_6S$: C, 43.56; H, 5.07; N, 15.63; S, 8.95%.

5-*Amino*-1-(5′-*azido*-5′-*deoxy*-2′,3′-O-*isopropylidene*-β-D-*ribofuranosyl*)-4-*cyano*-*imidazole* (**3**). To a solution of **2** (2.04 g) in acetonitrile (70 m*l*) was added sodium azide (4.07 g) and the mixture was refluxed for 15 hr under stirring. The precipitates were filtered off and the filtrate was evaporated. The residue was placed on a silica gel column (110 g, 2.7×48.5 cm) with a small amount of acetonitrile and eluted with benzene and benzene-acetone (4:1 and 3:1), successively. The eluents containing **3** were evaporated to afford crystals of **3**, yield 1.53 g (88.3%). An analytical sample was obtained by recrystallization from ethyl acetate: mp 138-139°C; $[\alpha]_D^{22}$-59° (c 1.4, methanol); ν_{max}^{KBr} 2215, 2110, 1662 and 1593 cm^{-1}; λ_{max}^{MeOH} 247 mμ (ε 13870); τ ($CDCl_3$) 2.75 (s, H-2), 4.37 (d, H-1′, $J_{1',2'}$=3.3 Hz), 6.25 (d, d, H-5′, $J_{4',5'}$=3.6 Hz, $J_{5a',5b'}$=1.7 Hz), 8.40 and 8.60 (s, $=C(CH_3)_2$).

Found: C, 47.35; H, 5.09; N, 31.73%. Calcd for $C_{12}H_{15}N_7O_3$: C, 47.21; H, 4.95; N, 32.11%.

5-*Amino*-1-(5′-*azido*-5′-*deoxy*-2′,3′-O-*isopropylidene*-β-D-*ribofuranosyl*)-4-*carbamoylimidazole* (**4**). To an ice-cooled solution of **3** (582 mg) in methanol (10 m*l*) was added 15N ammonium hydroxide (10 m*l*) and 30% hydrogen peroxide (2.5 m*l*). The mixture was stirred for 4 hr at room temperature and then palladium black was added to decompose hydrogen peroxide. After stirring for 30 min, the catalyst was filtered off and the filtrate was evaporated. The residue was dissolved in a small amount of acetone, placed on a silica gel column (20 g, 2.0×12.5 cm) and eluted with benzene and benzene-acetone (3:1). The eluents containing **4** were evaporated to afford a yellow glass; yield 397 mg (64.4%); ν_{max}^{KBr} 3400(sh), 3300, 2095, 1750, 1700(sh), 1637 and 1552 cm^{-1}; λ_{max}^{MeOH} 264 mμ.

5-*Amino*-1-(5′-*amino*-5′-*deoxy*-2′, 3′-O-*isopropylidene*-β-D-*ribofuranosyl*) *imidazole* (**5**). To a solution of **4** (397 mg) in methanol (6 m*l*) was added palladium black and the mixture was hydrogenated at 50 psi of hydrogen for 5 hr at room temperature. The catalyst was filtered off and the filtrate was evaporated to give **5** as a glass; yield 354 mg (97.6%); λ_{max}^{MeOH} 265 mμ.

5-*Amino*-1-(5′-*amino*-5′-*deoxy*-β-D-*ribofuranosyl*)-4-*carbamoylimidazole* (**6**). A solution of **5** (354 mg) in 30% acetic acid (22 m*l*) was heated for 5 hr at 85°C and then evaporated. The residue was dissolved in water and neutralized with Dowex 1×2 (OH type). The resin was removed by filtration and the brown filtrate was treated with activated charcoal. After removal of charcoal by filtration, the filtrate was evaporated to give **6** as a glass quantitatively: λ_{max}^{MeOH} 265 mμ; τ(D_2O) 2.47 (s, H-2), 4.29 (d, H-1′, $J_{1',2'}$=5.1 Hz). A solution of **6** (92 mg) in a small amount of water was added to a saturated aqueous picric acid solution (14 m*l*). The precipitated picrate of **6** was collected by filtration, yield 166 mg (62.5%). An analytical sample was obtained by recrystallization from methanol: mp 147°C (colored), 197°C (dec.), $[\alpha]_D^{22}$-5° (c 1.0, dimethylsulfoxide); ν_{max}^{KBr} 3280, 3130, 1675, 1607 and 1544 cm^{-1}, λ_{max}^{MeOH} 237 mμ (ε 29600).

Found: C, 35.27; H, 3.34; N, 21.30%. Calcd for $C_{21}H_{21}N_{11}O_{18}$: C, 35.25; H, 2.96; N, 21.54%.

5-*Amino*-1-(5′-*amino*-5′-*deoxy*-2′,3′-O-*isopropylidene*-β-D-*ribofuranosyl*)-4-*cyano*-

imidazole (**7**). Compound **3** was hydrogenated by the same procedure as described for the preparation of **5** to give **7** as a glass, yield 1.10 g (86.3%), λ_{max}^{MeOH} 248 mμ.

5-*Amino*-1-(5′-*amino*-5′-*deoxy*-β-D-*ribofuranosyl*)-4-*cyanoimidazole* (**8**). Compound **7** (1.10 g) was treated with 30% acetic acid by the same procedure as described for the preparation of **6**. The acetate of **8** was obtained as crystals quantitatively. An analytical sample was obtained by recrystallization from ethanol-ether: mp 168–170°C (colored); $[\alpha]_D^{22}$ −36° (c 1.4, water); ν_{max}^{KBr} 3420, 3140, 2190, 1665, 1603 and 1575 cm^{-1}; $\lambda_{max}^{0.1N\ HCl}$ 240 mμ (ε 8700), $\lambda_{max}^{H_2O}$ 244 mμ (ε 11680), $\lambda_{max}^{0.1N\ NaOH}$ 245 mμ (ε 10320); τ(D_2O) 2.44 (s, H-2), 4.30 (d, H-1′, $J_{1',2'}$=4.9 Hz), 8.09 (s, acetate).

Found: C, 44.02; H, 6.01; N, 23.57%. Calcd for $C_{11}H_{17}N_5O_5$: C, 44.14; H, 5.73; N, 23.40%.

5-*Amino*-4-*cyano*-1-(5′-*deoxy*-5′-*iodo*-2′, 3′-O-*isopropylidene*-β-D-*ribofuranosyl*)-*imidazole* (**9**). To a solution of **2** (1.80 g) in acetonitrile (45 m*l*) potassium iodide (10.8 g) was added and the mixture was refluxed for 5 hr under stirring. The precipitate was filtered off and the filtrate was evaporated. The residue was extracted with acetone and the extracts were again evaporated. The residue was placed on a silica gel column (120 g, 3.0×32.5 cm) and eluted with benzene and benzene-acetone (5:1). The eluents containing **9** were evaporated to give crystals, yield 1.56g (79.5%). An analytical sample was obtained by recrystallization from ethanol-ether: mp 158–160°C; $[\alpha]_D^{22}$ −88° (c 1.5, methanol); ν_{max}^{KBr} 3400, 3145, 2205, 1660 and 1589 cm^{-1}; λ_{max}^{MeOH} 245 mμ (ε 12800); τ($CDCl_3$) 8.63 (s, H-2), 4.36 (d, H-1′, $J_{1',2'}$=3.8 Hz), 4.95 (d, d, H-2′ $J_{2',3'}$=6.9 Hz), 5.25 (d, d, H-3′, $J_{3',4'}$=3.1 Hz), 5.81 (t, d, H-4′, $J_{4',5'}$=4.8 Hz), 6.58 (d, H-5′), 8.39 and 8.60 (s, =C(CH_3)$_2$).

Found: C, 37.05; H, 3.58; N, 14.78%. Calcd for $C_{12}H_{15}N_4O_3I$: C, 36.93; H, 3.88; N, 14.35%.

5-*Amino*-4-*cyano*-1-(5′-*deoxy*-2′, 3′-O-*isopropylidene*-β-D-*ribofuranosyl*) *imidazole* (**10**). To a solution of **9** (1.56 g) in 0.228N potassium hydroxide-methanol (17.2 m*l*) was added palladium black and the mixture was shaken at 50 psi of hydrogen for 3 hr at room temperature. After removal of the catalyst, the filtrate was evaporated. The residue was dissolved in a small amount of acetone, placed on a silica gel column (100 g, 2.7×36.5 cm) and eluted with benzene and benzene-acetone (3:1). The eluents containing **10** were evaporated to afford crystals, yield 985 mg (93.5%). Recrystallization from ethanol gave an analytical sample: mp 135°C (sintered); $[\alpha]_D^{20}$ +35° (c 1.0, methanol); ν_{max}^{KBr} 3400, 3220, 2210 and 1606 cm^{-1}; λ_{max}^{MeOH} 247 mμ (ε 14680); τ($CDCl_3$) 2.76 (s, H-2), 4.45 (d, H-1′, $J_{1',2'}$=3.3 Hz), 8.40 and 8.63 (s, =C(CH_3)$_2$), 8.64 (d,H-5′, $J_{4',5'}$= 6.4 Hz),

Found: C, 54.81; H, 5.72; N, 21.40%. Calcd for $C_{12}H_{16}N_4O_3$: C, 54.55; H, 6.10; N, 21.20%.

5-*Amino*-4-*cyano*-1-(5′-*deoxy*-β-D-*ribofuranosyl*) *imidazole* (**11**). A solution of **10** (480 mg) in 30% acetic acid (12 m*l*) was heated at 80°C for 2.5 hr and evaporated to afford crystals of **11** quantitatively. An analytical sample was obtained by recrystallization from ethanol: mp 268–270°C; $[\alpha]_D^{20}$ +74° (c 1.0, methanol); ν_{max}^{KBr} 3360, 3120, 2180, 1665 and 1590 cm^{-1}: $\lambda_{max}^{0.1N\ HCl}$ 252 mμ (ε 11200), $\lambda_{max}^{H_2O}$ 250 mμ (ε 11300), $\lambda_{max}^{0.1N\ NaOH}$ 252 mμ (ε 11380); τ(CD_3OD) 2.46 (s, H-2), 4.03 (d, H-1′, $J_{1',2'}$=7.9 Hz), 8.54 (d, H-5′, $J_{4',5'}$=9.3 Hz).

Found: C, 46.74; H, 5.51; N, 23.83%. Calcd for $C_9H_{12}N_4O_3 \cdot 1/2H_2O$: C, 46.35; H, 5.58; N, 24.03%.

5-*Amino*-4-*carbamoyl*-1-(5′-*deoxyl*-2′, 3′-O-*isopropylidene*-β-D-*ribofuranosyl*)-*imidazole* (**12**). Treatment of **10** (884 mg) with 15N ammonium hydroxide and 30% hydrogen peroxide as described for the preparation of **4** gave **12** as a glass, yield 550 mg (58.2%), λ_{max}^{MeOH} 226 mμ.

5-*Amino*-4-*carbamoyl*-1-(5′-*deoxy*-β-D-*ribofuranosyl*) *imidazole* (**13**). Treatment of **12** (550 mg) with 30% acetic acid as described for the preparation of **5** afforded **13** as a glass, yield 335 mg (71.0%). Crystallization from ethanol: mp 201–203°C (colored); $[\alpha]_D^{20}$ −53° (c 2.9, water); ν_{max}^{KBr} 3415, 3330 and 1640 cm^{-1}; $\lambda_{max}^{0.1N\ HCl}$ 268 mμ (ε 10200), $\lambda_{max}^{H_2O}$ 266 mμ (ε 12300), $\lambda_{max}^{0.1N\ NaOH}$ 267 mμ (ε 15320); τ(D_2O) 2.46 (s, H-2), 4.36 (d, H-1′, $J_{1',2'}$=5.5 Hz), 5.39 (d, d, H-2′, $J_{2',3'}$=5.5 Hz), 8.61 (d, H-5′, $J_{4',5'}$=6.4 Hz).

Found: C, 44.77; H, 5.89; N, 22.94%. Calcd for $C_9H_{14}N_4O_4$: C, 44.62; H, 5.83; N, 23.13%.

5-*Amino*-1-(5′-*acetylthio*-5′-*deoxy*-2′, 3′-O-*isopropylidene*-β-D-*ribofuranosyl*)-4-*cyanoimidazole* (**14**). To a solution of **2** (1.53 g) in acetonitrile (50 m*l*) potassium thioacetate (1.53 g) was added and the mixture was refluxed for 1 hr under stirring. The precipitate was filtered off and filtrate was evaporated with silica gel (1.5 g). The powdered residue was placed on a silica gel column (100 g, 3.0×33 cm) and eluted with benezene and benzene-acetone (4:1). The eluent containing **14** was evaporated to afford crystals, yield 1.39 g (95.6%). An analytical sample was obtained by recrystallization from ethyl acetate-diisopropyl ether. This crystals were positive in tetrazolium test (Trevelyan, Procter, et al. 1950; Wistler and Rowell, 1964) on TLC: mp 158–160°C; $[\alpha]_D^{21}$ −98° (c 1.4, methanol); ν_{max}^{KBr} 3430, 3160, 2205, 1703, 1646 and 1588 cm^{-1}; λ_{max}^{MeOH} 242 mμ (KOCH, 1949) (ε 15100); τ($CDCl_3$) 2.74 (s, H-2), 4.41 (d, H-1′, $J_{1',2'}$=3.5 Hz), 4.97 (d, d, H-2′, $J_{2',3'}$=6.7 Hz), 5.40 (d, d, H-3′, $J_{3',4'}$=3.3 Hz), 5.65 (t, d, H-4′, $J_{4',5'}$=5.7 Hz), 6.78 (d, H-5′), 7.60 (s, $SCOCH_3$), 8.39 and 8.63 (s, $=C(CH_3)_2$).

Found: C, 49.90; H, 5.51; N, 16.30; S, 9.03%. Cacld for $C_{14}H_{18}N_4O_4S$: C, 49.69; H, 5.36; N, 16.56; S, 9.48%.

5′, 5′-*Dithiobis* [5-*amino*-4-*cyano*-1-(5′-*deoxy*-2′, 3′-O-*isopropylidene*-β-D-*ribofuranosyl*) *imidazole*] (**15**). Method A: To a solution of **14** (1.323 g) in methanol (15 m*l*) was added 15N ammonium hydroxide (16 m*l*) and 35% hydrogen peroxide (4.1 m*l*) and the mixture was stirred for 2 hr. The crystalline precipitate of **15** was collected by filtration, yield 1.11 g (82.8%): mp 252–254°C; $[\alpha]_D^{20}$ −144° (c 1.5, dimethylsulfoxide); ν_{max}^{KBr} 3405, 3180, 2210, 1646 and 1587 cm^{-1}; λ_{max}^{MeOH} 248 mμ; τ(DMSO-d_6) 2.45 (s, H-2), 4.14 (d, H-1′, $J_{1',2'}$=2.8 Hz), 4.74 (d, d, H-2′, $J_{2',3'}$=6.5 Hz), 5.09 (d, d, H-3′, $J_{3',4'}$=6.1 Hz), 5.69 (t, d, H-4′, $J_{4',5'}$=7.0 Hz), 7.06 (d, H-5′), 8.49 and 8.65 (s, $=C(CH_3)_2$).

Found: C, 48.85; H, 5.42; N, 18.63; S, 10.58%. Calcd for $C_{24}H_{30}N_8O_6S_2$: C, 48.80; H, 5.12; N, 18.97; S, 10.85%.

This crystals were negative in triphenyltetrazolium test on TLC. Method B: A solution of **14** (100 mg) in 20% ammonia-methanol (6 m*l*) was kept in an ice bath for 7 hr and then at 47°C for 15 hr. The crystalline precipitate of **15** was collected by filtration, yield 69 mg (79.1%). The Rf value in TLC and IR spectrum of this specimen were identical with the above-mentioned disulfide **15** and triphenyltetrazolium test is negative.

5-*Amino*-1-(5′-*acetylthio*-5′-*deoxy*-β-D-*ribofuranosyl*)-4-*cyanoimidazole* (**16**). Treatment of **14** (914 mg) with 30% acetic acid as described for the preparation of **11** gave crystals contaminated with a syrup. The crystals of **16** were separated by filtration and washed with ethyl acetate, yield 481 mg. The filtrate and washings were com-

bined and evaporated with silica gel (1 g). The powdery residue was placed on a silica gel column (15 g, 1.8×15.5 cm) and eluted with ethyl acetate and ethyl acetete-ethanol (8:1, 4:1 and 2:1). The eluents containing **16** were evaporated to give crystals, yield 280 mg. Total yield of **16** was 761 mg (88.7%). An analytical sample was obtained by recrystallization from water: mp 118-120°C (dec.), $[\alpha]_D^{21}$ −33° (c 1.1, dimethylsulfoxide); ν_{max}^{KBr} 3410, 3330, 3110, 2190, 1692, 1593 and 1562 cm^{-1}; $\lambda_{max}^{0.1N\ HCl}$ 236 mμ (Koch, 1949) (ε 14320), $\lambda_{max}^{H_2O}$ 237 mμ (ε 14550), $\lambda_{max}^{0.1N\ NaOH}$ 242 mμ (ε 13100); $\tau(D_2O)$ 2.41 (s, H-2), 4.36 (d, H-1′, $J_{1',2'}$=4.9 Hz), 6.69 (d, H-5′, $J_{4',5'}$=4.7 Hz) and 7.62 (s, $SCOCH_3$).

Found: C, 44.59; H, 4.99; N, 18.60; S, 10.52%. Calcd for $C_{11}H_{14}N_4O_4S$: C, 44.29; H, 4.73; N, 18.78; S, 10.75%.

The authors wish to thank Mr. S. NAKADA for microanalyses and the Ajinomoto Co., Inc. for the generous supply of the AICAR.

REFERENCES

GREENBERG, G. R. and SPILMAN, E. L., (1956): Isolation of 5-Amino-4-imidazole Riboside, *J. Biol. Chem.*, **219**, 411.

HAYASHI, A., KUMAGAI, K., and KURETANI, K., (1968): Studies of Antitumor Agents I: Antitumor Activity of 5(4)-Amino-4(5)-imidazolecarboxamide Analogs, *Chem. Pharm. Bull.*, **16**, 2080.

KOCH, H. P., (1949): Absorption Spectra and Structure of Organic Sulphur Compounds. Part I: Unsaturated Sulphides, *J. Chem. Soc.*, 387.

MONTGOMERY, J. A., and THOMAS, H. J., (1969): 2-Aza-Adenosine (4-amino-7-β-D-ribofuranosyl-7*H*-imidazo [4,5-*d*]-*v*-triazine, *Chem. Commun.*, 458.

SHIRO, T., YAMANOI, A., KONISHI, S., OKAMURA, S. and TAKAHASHI, M. (1962): Ac cumulation of 5(4)-Amino-4(5)-imidazolecarboxamide Riboside by Base Auxotroph of Bacillus subtilis, *Agr. Biol. Chem.* **26**, 785.

TREVELYAN, W. E., PROCTER, D. P., and HARRISON, J. S., (1950): Detection of Sugars on Paper Chromatograms, *Nature*, **166**, 444.

WIBERG, K. W., (1953): The Mechanism of Hydrogen Peroxide Reactions. I: The Conversion of Benzonitrile to Benzamide, J. *Am. Chem. Soc.*, **75**, 3961.

WISTLER, R. L. and ROWELL, R. M., (1964). Preparation of Methy L-Arabinothiapyranoside and Disulfide Derivatives of 5-Mercapto-L-arabinose, *J. Org. Chem.*, **29**, 1259.

YAMAZAKI, A., KUMASHIRO, I., and TAKENISHI, T., (1967): Synthesis of Guanosine and Its Derivatives from 5-Amino-1-β-D-ribofuranosyl-4-imidazolecarboxamide. II: Ring Closure with Sodium Methylxanthate, *J. Org. Chem.*, **32**, 3032.

YAMAZAKI, A., KUMASHIRO, I., TAKANISHI, T. and IKEHARA, M. (1968): Synthesis of Thio-AICAR, 6-Thioxanthine, Isoguanine Analogs, and their Ribosides, *Chem. Pharm. Bull.*, **16**, 2172.