Sang-Gyeong Lee, Deok-Heon Kweon and Yong-Jin Yoon*

Department of Chemistry and Research Institute of Natural Sciences,
Gyeongsang National University, Chinju 660-701, Korea
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This paper presents the synthesis of novel pyridazine nucleosides containing the dicyanomethylene group and pyrrolo[2,3-*c*]pyridazine nucleoside.

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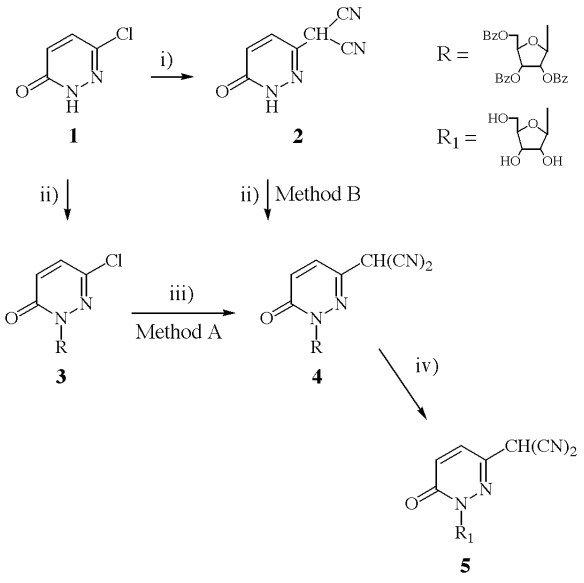
The synthesis and the biological activity of some pyridazine nucleosides as the isosteric analogs of uridine have been reported [1-6]. We also reported the synthesis of some bicyclic pyridazine nucleosides [7] and pyridazine acyclonucleosides [8,9].

In connection with our research program for the synthesis of multicyclic *N*-nucleosides containing the pyridazine ring, we need some pyridazine nucleosides containing dicyanomethylene at the 3- or 4-position of the pyridazine ring.

In the present paper, we would like to report the synthesis of 3- or 4-dicyanomethylenepyridazin-6-one and pyrrolo[2,3-*c*]pyridazin-3(2*H*)-one nucleosides from chloropyridazin-6-ones or the corresponding nucleosides.

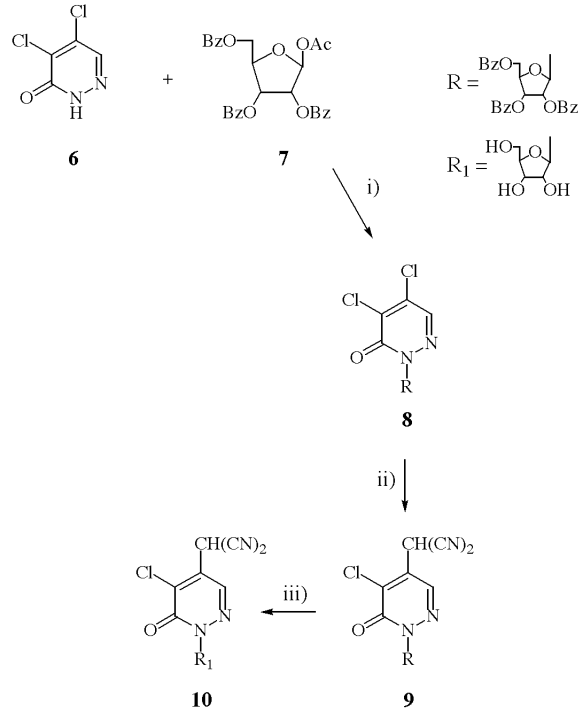
Reaction of **3** [5] with malononitrile in the presence of sodium hydride in dimethyl sulfoxide at room temperature gave **4** in low yield (Method A). Ribosylation of **2** [6] with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose was also accomplished by the stannic chloride catalyzed procedure to give **4** in 70% yield (Method B). Debenzoylation of **4** with methanolic sodium methoxide furnished **5** in 91% yield. The structures of **4** and **5** were established by ir, pmr and elemental analyses. The infrared spectra of **4** and **5** showed the absorption bands of two cyano groups at 2170 and 2210 cm^{-1}, one amide carbonyl group at 1640 cm^{-1} and one ester carbonyl group for **4** at 1725 cm^{-1}. The pmr spectra of **4** and **5** also revealed the signals of two protons on the pyridazine ring and protons for the sugar moiety, however the signal of one proton for dicyanomethylene was not detected. This may be due to broadening by nitrogen and tautomerization of dicyanomethylenepyridazinone [10].

Scheme I



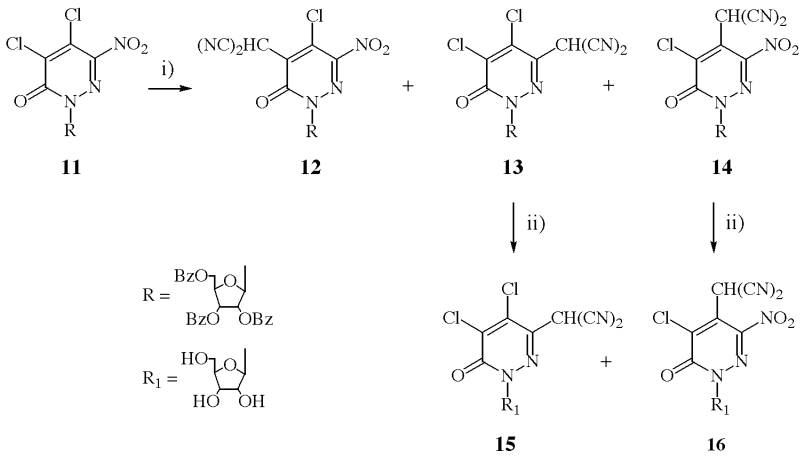
i) $CH_2(CN)_2$, tetrahydrofuran, NaH. ii) 1) Ammonium sulfate, hexamethyldisilazane, 1-*O*-acetyl-2,3,4-tri-*O*-benzoyl-β-D-ribofuranose $SnCl_4$, 1,2-dichloroethane, 2) Sodium bicarbonate, ethanol. iii) $CH_2(CN)_2$, NaH, DMSO. iv) 1) NaOMe, MeOH 2) Amberlite IRC-50H$^+$.

Scheme II



i) 1) Ammonium sulfate, hexanemethyldisilazane, 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl β-D-ribofuranose, $SnCl_4$, 1,2-dichloroethane, 2) sodium bicarbonate, ethanol. ii) $CH_2(CN)_2$, NaH, DMSO. iii) NaOMe, MeOH, Amberlite IRC-50H$^+$.

Scheme III



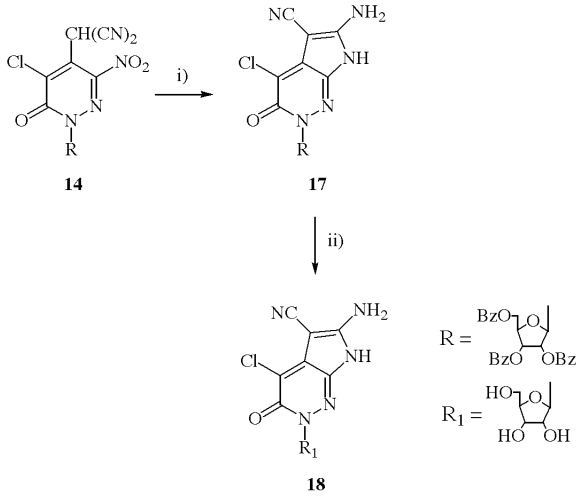
i) NaH, $CH_2(CN)_2$, DMSO. ii) 1) NaOMe, MeOH, 2) Amberlite IRC-50H$^+$.

Treatment of **8** [5] with malononitrile in the presence of sodium hydride in dimethyl sulfoxide afforded **9** in 74% yield. The position of dicyanomethylene group on the pyridazine ring was determined by the further reactions of **9** [11]. Debenzoylation of **9** with methanolic sodium methoxide gave compound **10** in 92% yield. The structures of **9** and **10** were established by spectral and elemental analytical data. The infrared spectrum of **10** showed the absorption bands of two cyano groups (for **9**: 2200, 2160 cm^{-1}, for **10**: 2200, 2170 cm^{-1}) and carbonyl groups (for **9**: 1700, 1620 cm^{-1}, for **10**: 1620 cm^{-1}). The pmr spectra of **9** and **10** showed the proton signals for the pyridazine ring (at 3-position) and sugar moiety, however the proton signal of dicyanomethylene was not detected.

On the other hand, reaction of **11** [5] with malononitrile in the presence of sodium hydride in dimethyl sulfoxide furnished **12** (5%), **13** (19%) and **14** (49%), respectively. The structures of **12**, **13**, and **14** were assigned on the basis of spectral and elemental analytical data. The infrared spectra of **12** and **14** showed the absorption bands corresponding to the nitro group at 1550 and 1350 cm^{-1}, whereas for **13** the absorption bands of the nitro group were not detected. The position of the dicyanomethylene group of **14**, however, could not establish by the spectral and elemental analytical data. Therefore, we carried out a cyclization of **14** in order to establish the position of dicyanomethylene group.

The reductive cyclization of **14** with stannous chloride dihydrate/sodium borohydride (1:1 mole ratio) in ethyl acetate furnished selectively **17** in 63% yield. The conversion of **14** to **17** is corroborative evidence for the structure of **14**. Debenzoylation of **13**, **14** and **17** with methanolic sodium methoxide gave the corresponding nucleosides **15** (90%), **16** (88%) and **18** (73%), respectively. The structures of **15**, **16** and **18** were established by spectral and elemental analytical data. The infrared spectrum of **18** showed the absorption bands of one cyano group at 2200 cm^{-1} and one amide carbonyl group at 1660 cm^{-1}. The pmr spectrum of **18** also revealed the signals of NH at δ 11.95 ppm and NH_2 at δ 8.48 ppm.

Scheme IV



i) $NaBH_4$, $SnCl_2 \cdot 2H_2O$, EtOAc, Reflux. ii) 1) NaOMe, MeOH, 2) Amberlite IRC-50H$^+$.

3-Nitro-4-dicyanomethylenepyridazin-6-one derivative is a useful material for the synthesis of some bi- or tricyclic heterocycles involving pyridazine such as pyrrrolo[2,3-*c*]-pyridazin-3(2*H*)-one derivative.

Further work including the chemical transformation and biological activity of novel nucleosides is under way in our laboratory.

EXPERIMENTAL

Melting points were determined with a Thomas-Hoover capillary apparatus and are uncorrected. Magnetic resonance spectra were obtained on a Varian Unity Plus 300 MHz spectrometer with chemical shift values reported in δ units (part per million) relative to an internal standard (tetramethylsilane). Infrared spectral data were obtained on a Hitachi 270-50 spectrophotometer. Elemental analyses were performed with a Perkin Elmer 240C. The presence of water of crystal in the elemental analyses was verified by pmr spectroscopy. Nucleosides were detected by treatment with sulfuric acid followed by charring. Open-bed chromatography was carried out on silica gel 60 (70-230 mesh, Merck) using gravity flow. The column was packed as slurries with the elution solvent.

3-Dicyanomethylene-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyridazin-6-one (**4**).

Method A.

A mixture of malononitrile (0.45 g, 6.8 mmoles), sodium hydride (0.3 g, 7.5 mmoles, 60% in oil) and dry dimethyl sulfoxide (15 ml) was stirred for 0.5 hours at room temperature under a nitrogen atmosphere. The solution of **3** [5] (2 g, 3.48 mmoles) in dry dimethyl sulfoxide (10 ml) was added to the above mixture, and the reaction mixture was stirred for 43 hours at room temperature under nitrogen atmosphere. The reaction was quenched by the addition of aqueous acetic acid (10%, 30 ml), and the reaction mixture was then stirred for an additional 0.5 hours at room temperature. After the mixture was poured into water (200 ml), the product was extracted with ethyl acetate (200 ml x 3). The extract was washed with water (100 ml x 4), and dried over anhydrous magnesium sulfate and filtered. The filtrate was coevaporated with silica gel (4 g), and applied to the top of an open-bed silica gel column (2.0 x 45 cm). The column was eluted with chloroform/methanol (8.5:1.5, v/v). The fractions containing the product were combined and evaporated under reduced pressure to furnish **4** as dark brown powder in 43% (0.85 g) yield. Recrystallization of a small sample from ethyl acetate yielded an analytical sample as powder, mp 216-218°; ir (potassium bromide) 2210, 2170, 1725, 1640 cm^{-1}. ^1H nmr (DMSO-d_6): δ 4.71 (m, $1H_{4'}$ + $2H_{5'}$), 6.04 (m, $1H_{2'}$ + $1H_{3'}$), 6.60 (d, $1H_{1'}$, $J_{1',2'}$ = 4), 7.55 ppm (m, $1H_4$ + $1H_5$ + benzoyl-5H).

Anal. Calcd. for $C_{33}H_{24}N_4O_8$•1(1/2)H_2O: C, 62.76; H, 4.31; N, 8.87: Found; C, 62.61; H, 4.10; N, 8.71.

Method B.

3-Dicyanomethylenepyridazin-6-one (**2**, 0.6 g, 3.75 mmoles) [6] was silylated by refluxing for 3 hours in hexamethyldisilazane (20 ml) in the presence of a catalytic amount of ammonium sulfate. The excess hexamethyldisilazane was removed by distillation under reduced pressure, and the resulting residue was used without further purification. The silylated pyridazine and 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (1.8 g, 3.57 mmoles) were dissolved in dry dichloroethane (40 ml), and the solution was cooled to 5°. Stannic chloride (1 ml, 8.89 mmoles) was added, and the solution was then refluxed for 40 minutes. After cooling the mixture to 0°, ethanol (10 ml) and sodium bicarbonate (2.7 g) were then added with stirring. The solvent was evaporated to dryness under reduced pressure. The residue was triturated with boiling ethyl acetate (50 ml x 2). After filtering the mixture, the filtrate was coevaporated with silica gel (4 g) under reduced pressure. The resulting silica gel was applied to the top of an open-bed silica gel column (2.5 x 30 cm). The column was eluted with chloroform/methanol (8:2, v/v). After discarding the first eluent (130 ml), the eluent was collected in 6 ml fraction. The fractions containing the product were combined and evaporated under reduced pressure to give **4** as dark brown powder in 70% (1.67 g) yield. Recrystallization of a small sample from ethyl acetate yielded an analytical sample as powder. This product was identical with compound **4** that was prepared by the Method A.

3-Dicyanomethylene-1-β-D-ribofuranosylpyridazin-6-one (**5**).

Benzoylated nucleoside **4** (0.7 g, 1.16 mmoles) was dissolved in methanol (150 ml). After adding sodium methoxide (0.9 g, 15.8 mmoles, 95%), the mixture was then stirred for 48 hours at room temperature. Amberlite IRC-50 (H^+ form, 1.5 g) was added to the solution, and the mixture was then stirred for an additional 24 hours at room temperature. The mixture was filtered and the resin was then washed with boiling methanol (50 ml). The combined filtrates were concentrated to about 5 ml. The resulting solution was applied to the top of an open-bed silica gel column (1.5 x 40 cm), and the column was then eluted with chloroform/methanol (7:3, v/v). The fractions containing nucleoside were combined and evaporated under reduced pressure to give **5** as dark brown powder in 91% (0.33 g) yield. Recrystallization of a small sample from ethanol yielded an analytical sample as powder, mp 294° (dec.); ir (potassium bromide) 2210, 2170, 1640 cm^{-1}. ^1H nmr (DMSO-d_6): δ 3.70 (m, $1H_{2'}$ + $1H_{3'}$ + $1H_{4'}$ + $2H_{5'}$), 5.01 (m, $OH_{2'}$ + $OH_{3'}$ + $OH_{5'}$, D_2O exchangeable), 6.18 (d, $1H_{1'}$, $J_{1',2'}$ = 4), 6.51 (d, $1H_5$, J = 8), 6.95 (d, $1H_4$, J = 8).

Anal. Calcd. for $C_{12}H_{12}N_4O_5$: C, 49.32; H, 4.14; N, 19.17. Found: C, 49.48; H, 4.39; N, 19.41.

5-Chloro-4-dicyanomethylene-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyridazin-6-one (**9**).

A mixture of malononitrile (0.325 g, 4.92 mmoles), sodium hydride (0.215 g, 5.37 mmoles, 60% in oil) and dry dimethyl sulfoxide (10 ml) was stirred for 0.5 hours at room temperature under nitrogen atmosphere. The solution of **8** [5] (2 g, 3.28 mmoles) in dry dimethyl sulfoxide (15 ml) was added to above mixture, and the reaction mixture was then stirred for 3.5 hours at room temperature under nitrogen atmosphere. The reaction was quenched by the addition of aqueous acetic acid (10%, 30 ml), and the mixture was then stirred for an additional 0.5 hours at room temperature. After the mixture was poured into water (200 ml), the product was extracted with ethyl acetate (100 ml x 4). The ethyl acetate solution was washed with water (200 ml x 4), and dried over anhydrous magnesium sulfate. The solution was coevaporated with silica gel (4 g) under reduced pressure. The resulting silica gel was applied to the top of an

open-bed silica gel column (2 x 40 cm). The column was eluted with chloroform/methanol (8.5:1.5, v/v). The fractions containing the product were combined and evaporated under reduced pressure to give **9** as dark brown powder in 74% (1.5 g) yield. Recrystallization of a small sample from ethyl acetate yielded an analytical sample powder, mp 221-223°; ir (potassium bromide) 2200, 2160, 1700, 1620 cm^{-1}. ^1H nmr (DMSO-d_6): δ 4.75 (m, $1H_{4'}$ + $2H_{5'}$), 6.05 (m, $1H_{2'}$ + $1H_{3'}$), 6.53 (d, $1H_{1'}$, $J_{1',2'}$ = 2), 7.65 (m, $1H_3$ + benzoyl-5H).

Anal. calcd. for $C_{33}H_{23}N_4O_8Cl•1/2H_2O$; C, 61.16; H, 3.73; N, 8.65: Found; C, 61.09; H, 4.00; N, 8.80.

5-Chloro-4-dicyanomethylene-1-β-D-ribofuranosylpyridazin-6-one (**10**).

Benzoylated nucleoside **9** (1.6 g, 2.51 mmoles) was dissolved in methanol (60 ml). After adding sodium methoxide (0.9 g, 15.8 mmoles, 95%) to the solution, the mixture was then stirred for 14 hours at room temperature. Amberlite IRC-50 (H^+ form, 1.7 g) was added, and the mixture was then stirred for an additional 24 hours at room temperature. The mixture was filtered, and the resin was washed with boiling methanol (50 ml). The combined filtrates were coevaporated with silica gel (2 g) under reduced pressure. The resulting silica gel was applied to the top of an open-bed silica gel column (1.5 x 40 cm), and the column was then eluted with ethyl acetate/methanol (8:2, v/v). The fractions containing nucleoside were combined and evaporated under reduced pressure to give **10** as dark brown powder in 92% (0.75 mg) yield. Recrystallization of a small sample from ethanol yielded an analytical sample as powder, mp 250° (dec.); ir (potassium bromide) 2200, 2170, 1620 cm^{-1}. ^1H nmr (DMSO-d_6): δ 3.95 (m, $1H_{2'}$ + $1H_{3'}$ + $1H_{4'}$ + $2H_{5'}$), 4.63 (t, $OH_{5'}$, D_2O exchangeable), 4.90 (d, $OH_{3'}$, J = 4, D_2O exchangeable), 5.28 (d, $OH_{2'}$, J = 4, D_2O exchangeable), 6.20 (d, $1H_{1'}$, J = 2), 8.10 (s, $1H_3$).

Anal. calcd. for $C_{12}H_{11}N_4O_5Cl$; C, 44.12; H, 3.39; N, 17.15. Found: C, 44.29; H, 3.65; N, 17.37.

4-Chloro-5-dicyanomethylene-3-nitro-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyridazin-6-one (**12**), 4,5-Dichloro-3-dicyanomethylene-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl) pyridazine-6-one (**13**) and 5-Chloro-4-dicyanomethylene-3-nitro-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyridazin-6-one (**14**).

A mixture of malononitrile (0.33 g, 4.99 mmoles), sodium hydride (0.207 g, 5.18 mmoles, 60% in oil) and dry dimethyl sulfoxide (10 ml) was stirred for 0.5 hours at room temperature under nitrogen atmosphere. The solution of **11** [5] (2.5 g, 3.82 mmoles) in dry dimethyl sulfoxide (10 ml) was added to the above mixture, and the reaction mixture was then stirred for 6 hours at room temperature under nitrogen atmosphere. The reaction was quenched by the addition of aqueous acetic acid (10%, 40 ml), and the mixture was then stirred for an additional 0.5 hours at room temperature. After the mixture was poured into water (100 ml), the product was extracted with ethyl acetate (100 ml x 4). The organic solution was washed with water (200 ml x 4), and dried over anhydrous magnesium sulfate. The solution was coevaporated with silica gel (5 g) under reduced pressure. The resulting silica gel was applied to the top of an open-bed silica gel column (2 x 45 cm). The column was eluted with chloroform/methanol (8.5:1.5, v/v). After discarding the first fraction (150 ml), the eluent was collected in 6 ml fraction. Fractions 45-162 (Rf = 0.26, chloroform/methanol=8.5:1.5, v/v) were combined and evaporated under reduced pressure to give **14** as dark brown powder in 49% (1.29 g) yield. Recrystallization of a small sample from ethyl acetate yielded an analytical sample as powder, mp 204-206°; ir (potassium bromide) 2200, 2170, 1725, 1640, 1550, 1350 cm^{-1}. ^1H nmr (DMSO-d_6): δ 3.99 (m, $1H_{2'}$ + $1H_{3'}$ + $1H_{4'}$ + $1H_{5'}$), 4.48 (t, $OH_{5'}$, D_2O exchangeable), 4.91 (d, $OH_{3'}$, J = 5, D_2O exchangeable), 5.28 (d, $OH_{2'}$, J = 5, D_2O exchangeable), 6.55 ppm (d, $1H_{1'}$, J = 4).

Anal. calcd. for $C_{33}H_{22}N_5O_{10}Cl•1/2H_2O$; C, 57.19; H, 3.35; N, 10.11. Found: C, 57.18; H, 3.08; N, 10.07.

Fractions 186-215 (Rf = 0.21, chloroform/methanol = 8.5:1.5, v/v) were combined and evaporated under reduced pressure to give **13** as dark brown powder in 19% (0.5 g) yield. recrystallization of a small sample from ethyl acetate yielded an analytical sample as powder, mp 274-275°; ir (potassium bromide) 2200, 2170, 1720, 1640 cm^{-1}. ^1H nmr (DMSO-d_6): δ 4.60 (m, $1H_{4'}$ + $2H_{5'}$), 5.93 (m, $1H_{2'}$ + $1H_{3'}$), 6.65 (d, $1H_{1'}$, J = 2), 7.67 ppm (m, benzoyl-5H).

Anal. calcd. for $C_{33}H_{22}N_4O_8Cl_2•1/2H_2O$; C, 58.08; H, 3.40; N, 8.21. Found: C, 57.99; H, 3.44; N, 8.57.

Fractions 295-370 (Rf = 0.19, chloroform/methanol; 8.5:1.5, v/v) were combined and evaporated under reduced pressure to give **12** as dark brown powder in 5% (0.133 g) yield. Recrystallization of a small sample from ethyl acetate yielded an analytical sample as powder, mp 271-273°; ir (potassium bromide) 2200, 2190, 1720, 1650, 1550, 1350 cm^{-1}. ^1H nmr (DMSO-d_6): δ 4.66 (m, $1H_{4'}$ + $2H_{5'}$), 5.89 (m, $1H_{2'}$ + $1H_{3'}$), 6.50 (d, $1H_{1'}$, J = 2), 7.68 ppm (m, benzoyl-5H).

Anal. calcd. for $C_{33}H_{22}N_5O_{10}Cl•1/2H_2O$; C, 57.19; H, 3.35; N, 10.11. Found: C, 57.17; H, 3.21; N, 10.04.

4,5-Dichloro-3-dicyanomethylene-1-β-D-ribofuranosylpyridazin-6-one (**15**).

Benzoylated nucleoside **13** (0.4 g, 0.59 mmoles) was dissolved in methanol (30 ml). After adding sodium methoxide (0.5 g, 8.79 mmoles, 95%), the mixture was stirred for 22 hours at room temperature. Amberlite IRC-50 (H^+ form, 4 g) was added, and the mixture was then stirred for an additional 24 hours at room temperature. After filtering the mixture, the resin was washed with boiling methanol (50 ml). The combined filtrate was coevaporated with silica gel (3 g) under reduced pressure. The resulting silica gel was applied to the top of an open-bed silica gel column (1.5 x 40 cm), and the column was then eluted with chloroform/methanol (7:3, v/v). The fractions containing nucleoside were combined and evaporated under reduced pressure to give **15** as dark brown powder in 90% (0.24 g) yield. Recrystallization of a small sample from ethanol yielded an analytical sample as powder, mp 291° (dec.); ir (potassium bromide) 2210, 2170, 1650 cm^{-1}. ^1H nmr (DMSO-d_6): δ 4.66 (m, $1H_{4'}$ + $2H_{5'}$), 5.91 (m, $1H_{2'}$ + $1H_{3'}$), 6.52 (d, $1H_{1'}$, J = 2), 7.70 ppm (m, benzoyl-5H).

Anal. Cacd. For $C_{12}H_{10}N_4O_5Cl_2$; C, 39.91; H, 2.79; N, 15.51. Found: C, 39.67; H, 2.86; N, 15.87.

5-Chloro-4-dicyanomethylene-3-nitro-β-D-ribofuranosylpyridazin-6-one (**16**).

Benzoylated nucleoside **14** (1.2 g, 1.76 mmoles) was dissolved in methanol (50 ml). After adding sodium methoxide (0.5 g, 8.79 mmoles, 95%), the mixture was stirred for 19.5 hours at room temperature. Amberlite IRC-50 (H^+ form, 2 g) was added, and the mixture was then stirred for an additional 22 hours at

room temperature. After filtering the solution, the resin was washed with boiling methanol (50 ml). The combined filtrate was coevaporated with silica gel (3 g) under reduced pressure. The resulting silica gel was applied to the top of an open-bed silica gel column (1.5 x 40 cm), and the column was then eluted with ethyl acetate/methanol (9:1, v/v). The fractions containing nucleoside were combined and evaporated under reduced pressure to give **16** as dark brown powder in 88% (0.57 g) yield. Recrystallization of a small sample from ethanol yielded an analytical sample as powder, mp 273° (dec.); ir (potassium bromide) 2210, 2170, 1660, 1555, 1350 cm^{-1}. ^1H nmr (DMSO-d_6): δ 3.99 (m, $1H_{2'}$ + $1H_{3'}$ + $1H_{4'}$ + $2H_{5'}$), 4.48 (t, $OH_{5'}$, D_2O exchangeable), 4.98 (d, $OH_{3'}$, J = 4, D_2O exchangeable), 5.30 (d, $OH_{2'}$, J = 4, D_2O exchangeable), 6.55 ppm (d, $1H_{1'}$, J = 4).

Anal. calcd. for $C_{12}H_{10}N_5O_7Cl$; C, 38.78; H, 2.71; N, 18.84. Found: C, 38.97; H, 2.44; N, 19.13.

6-Amino-4-chloro-5-cyano-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3(2*H*)-one (**17**).

Compound **14** (1.5 g, 2.19 mmoles) was dissolved in ethyl acetate (200 ml). After adding sodium borohydride (0.3 g, 7.9 mmoles) and stannous chloride dihydrate (1.5 g, 7.9 mmoles), the mixture was refluxed for 22 hours. The mixture was cooled to room temperature and filtered. The filtrate was coevaporated with silica gel (3 g) under reduced pressure. The resulting silica gel was applied to the top of an open-bed silica gel column (2.5 x 30 cm). The column was eluted with ethyl acetate/*n*-hexane (7:3, v/v). The fractions containing the product were combined and evaporated to give **17** as beige powder in 63% (0.883 g) yield. Recrystallization of a small sample from ethyl acetate yielded an analytical sample as powder, mp 183-185°; ir (potassium bromide) 3400, 3300, 3200, 2200, 1720, 1650, 1570, 1455, 1450 cm^{-1}. ^1H nmr (DMSO-d_6): δ 4.63 (m, $1H_{4'}$ + $2H_{5'}$), 6.03 (m, $1H_{2'}$ + $1H_{3'}$), 6.69 (d, $1H_{1'}$, J = 2), 7.68 (m, benzoyl-5H), 8.48 (s, NH_2, D_20 exchangeable). 11.95 ppm (s, NH).

Anal. calcd. for $C_{33}H_{24}N_5O_8Cl•H_2O$; C, 58.98; H, 3.90; N, 10.42. Found; C, 58.81; H, 4.00; N, 10.39.

6-Amino-4-chloro-5-cyano-2-β-D-ribofuranosyl-7*H*-pyrrolo[2,3-*c*]pyridazin-3(2*H*)-one (**18**).

Nucleoside **17** (0.6 g, 9.24 mmoles) was dissolved in methanol (30 ml) and 1,2-dichloroethane (20 ml). After adding sodium methoxide (0.6 g, 10.55 mmoles, 95%), the mixture was stirred for 48 hours at room temperature. Amberlite IRC-50 (H^+ form, 1 g) was added, and the mixture was then stirred for an additional 48 hours at room temperature. The mixture was filtered, and the resin was washed with boiling methanol (50 ml). The combined filtrate was coevaporated with silica gel (2 g) under reduced pressure. The resulting silica gel was applied to the top of an open-bed silica gel column (1.5 x 40 cm), and the column was then eluted with ethyl acetate/methanol (6:4, v/v). The fractions containing nucleoside were combined and evaporated under reduced pressure to give **18** as dark brown powder in 73% (0.23 g) yield. Recrysatllization of a small sample from ethanol yielded an analytical sample as powder, mp 241-243°; ir (potassium bromide) 2200, 1660, 1450 cm^{-1}. ^1H nmr (DMSO-d_6): δ 4.60 (m, $1H_{4'}$ + $1H_{5'}$ + $OH_{5'}$, D_2O exchangeable), 4.95 (d, $OH_{3'}$, J = 4, D_2O exchangeable), 5.27 (d, $OH_{2'}$, J = 4, D_2O exchangeable), 5.99 (m, $1H_{2'}$ + $1H_{3'}$), 6.69 (d, $1H_{1'}$, J = 2), 8.48 (s, NH_2, D_2O exchangeable), 11.95 ppm (s, NH, D_2O exchangeable).

Anal. calcd, for $C_{12}H_{12}N_5O_5Cl$; C, 42.18; H, 3.54; N, 20.50. Found: C, 41.97; H, 3.90; N, 20.73.

Acknowledgements.

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