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Synthesis of *C*-Nucleosides by Ring Transformation of 1,3-Oxazine Derivatives[1)]

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Treatment of the β-D-ribofuranosyl cyanide **5** with sodium methoxide, followed by reaction with diketene, gave the spiro 1,3-oxazine **6**, which underwent the ring transformation with ammonia and phenylhydrazine to give the protected pyrimidine (**8**) and 1,2,4-triazole (**13**) *C*-nucleosides, respectively. Deprotection of **8** with 90% trifluoroacetic acid gave the pyrimidine *C*-nucleoside **9**. Passage of hydrogen chloride gas over a solution of the cyanide **1** and benzyl hydrosulfide gave the fully protected ribofuranosylthioformimidate **15**. Treatment of **15** with triethylamine, followed by reaction with diketene gave the dihydrofuran derivative **16**. Compound **16**, on treatment with ammonia, hydroxylamine, and phenylhydrazine, was transformed into the corresponding furan derivatives **17**—**19**.

Keywords——*C*-nucleoside; 1,3-oxazine; diketene; imidate; ring transformation; dihydrofuran; furan; pyrimidine

C-Nucleosides, having a carbon–carbon ribosidic linkage, have aroused much interest owing to their significant pharmacological activities.[2)] Previously, we have reported the synthesis of homo-*C*-nucleosides using pyrimidinylmethylenephosphoranes.[3)] We have also achieved the synthesis of pyrazofurin,[4)] an antibiotic *C*-nucleoside having antitumor and antiviral activities, and several related compounds. One of the latter *C*-nucleosides was found to be as potent in its antiviral activity as pyrazofurin itself.[5)]

On the other hand, recent studies on 1,3-oxazine chemistry have revealed that 1,3-oxazines are valuable compounds as synthetic intermediates.[6)] In particular, 1,3-oxazin-4-ones, which are easily prepared by the reaction of diketene with imido esters, serve as reagents for the syntheses of *N*-heterocycles such as pyridines and pyrimidines.[7)]

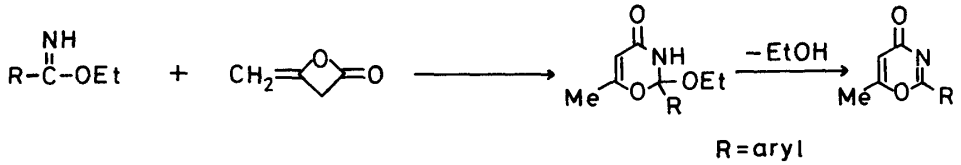

Chart 1

In connection with our continuing interests in *C*-nucleoside chemistry and with studies directed toward the synthesis of pharmacologically active substances, we wish to report the synthesis of *C*-nucleosides by ring transformation of 1,3-oxazine derivatives, which can be obtained from the reaction of diketene with ribofuranosyl formimidates.

Poonian and Nowoswiat[8)] have reported that treatment of 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl cyanide (**1**) with sodium methoxide gives the imido ester **2** as a stable crystalline substance which is available for the synthesis of *C*-nucleosides. This observation prompted us

to investigate the reaction of diketene with **2**. According to the reported procedure,[8] we prepared **2** by treatment of **1** with sodium methoxide and examined the reaction of **2** with diketene. Although we investigated the reaction conditions in detail, we could not obtain the desired 1,3-oxazine **3**, but instead obtained a complicated mixture that was inseparable by column chromatography. This undesirable result is probably attributable to the presence of three unprotected hydroxyl groups in **2**, resulting in low solubility in organic solvents.

Therefore, we sought to prepare the imido ester from 5-*O*-benzoyl-2,3-*O*-isopropylidene-*β*-D-ribofuranosyl cyanide (**5**), the 2,3-hydroxyl groups of which are protected by a protecting group stable to base. According to the procedure reported by Moffatt *et al.*,[9] **5** was prepared by selective deblocking of **1** with ammonia in methanol (preparation of compound **4**), followed by treatment with 2,2-dimethoxypropane in the presence of perchloric acid.

Treatment of **5** with sodium methoxide, followed by neutralization with ion exchange resin gave an oily substance which, without further purification, was reacted with diketene to give **6** as prisms in 18% yield. The spiro structure (**6**) was assigned to the product on the basis of the following spectral data. The infrared (IR) spectrum of **6** shows NH and carbonyl absorption bands at 3420 and 1680 cm^{-1}, respectively. The ^{1}H- and ^{13}C-nuclear magnetic resonance (NMR) data for **6** are listed in Table I. In the ^{1}H-NMR spectrum, the signals due to methyl protons, a ring proton, and NH of the 2,3-dihydro-1,3-oxazin-4-one were observed at δ 2.04, 5.25, and 8.48, respectively. The ^{13}C-NMR spectrum exhibited the signal due to the spiro carbon (2-position) at δ 100.75 (s). However, the configuration at the spiro position is not clear.

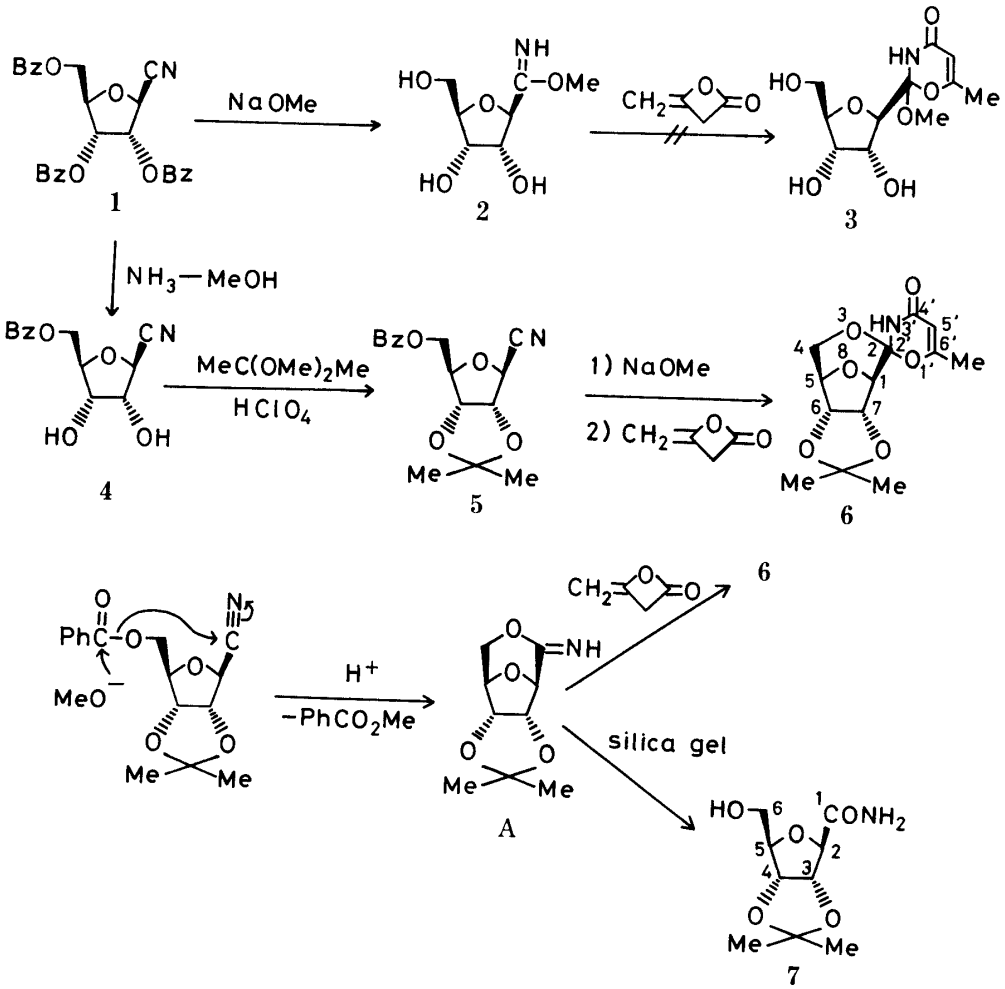

Chart 2

Table I. ^{1}H- and ^{13}C-NMR Spectral Data for Compound **6**

Position	Chemical shift (δ, ppm)	
	Proton	Carbon
1	4.28 (1H, s)	79.67 (d)[a]
2 (2′)	—	100.75 (s)
4	3.54 (1H, d, J=12 Hz)	64.88 (t)
	4.12 (1H, dd, J=12 Hz, 2 Hz)	
5	4.20 (1H, d, J=2 Hz)	83.07 (d)[a]
6	4.78 (1H, d, J=6 Hz)	82.43 (d)[a]
7	5.08 (1H, d, J=6 Hz)	81.90 (d)[a]
3′	8.48 (1H, br)	
4′	—	164.21 (s)[a]
5′	5.25 (1H, s)	98.40 (d)
6′	—	164.03 (s)[a]
6′-Me	2.04 (3H, s)	19.73 (q)
Isopropylidene-Me	1.35 (3H, s), 1.48 (3H, s)	24.60 (q), 25.95 (q)
Isopropylidene-C	—	112.55 (s)

a) Tentative assignment.

Compound **6** is presumably produced by the reaction of diketene with the cyclic imido ester A, formed by the attack of methoxide ion on the benzoyl carbonyl of **5**, followed by addition to the cyano group. In order to isolate A, the oily product obtained from **5** by treatment with sodium methoxide followed by neutralization was subjected to silica gel column chromatography. Instead of A, however, the amide **7** was obtained as the sole product.

Next, we investigated the ring transformation of **6** with the intention of obtaining *C*-nucleosides. When compound **6** was treated with liq. ammonia in abs. methanol in a sealed tube at room temperature, the protected pyrimidine *C*-nucleoside **8** was obtained in 80% yield. The structure was elucidated on the basis of spectral data as detailed in the experimental section. In particular, the configuration at the anomeric position of **8** was determined by ^{13}C-NMR spectroscopy. Namely, in the ^{13}C-NMR spectrum of **8**, signals due to two methyl carbons of the isopropylidene group are observed at δ25.36 and 27.36, within the range strongly indicative of the β configuration (25.5 ± 0.2 and 27.5 ± 0.2).[10] Deprotection of **8** with 90% trifluoroacetic acid gave the pyrimidine *C*-nucleoside **9** in 83% yield. In order to confirm the structure of **9**, we tried to synthesize **9** by another route.

Namely, the carboxylic acid **10**,[11] the β-anomer, was condensed with 3-aminocrotonamide[12] in the presence of dicyclohexylcarbodiimide (DCC) to give the amide **11** in 60% yield. Cyclization of **11** with trimethylsilyl chloride–hexamethyldisilazane (HMDS)[13] gave the protected pyrimidine *C*-nucleoside **12** in 96% yield. Deprotection of **12** with sodium methoxide gave the pyrimidine *C*-nucleoside **9**, whose IR spectrum was identical with that of an authentic sample obtained from **8**.

Yamamoto *et al.*[14] reported that 6-methyl-2-phenyl-1,3-oxazin-4-one underwent ring transformation with phenylhydrazine to give 5-(1,3-diphenyl-1*H*-1,2,4-triazolyl)acetone phenylhydrazone. Thus, we investigated the ring transformation of **6** with phenylhydrazine. When compound **6** was allowed to react with two mol eq of phenylhydrazine in ethanol under reflux, a protected 1,2,4-triazole *C*-nucleoside **13** was obtained in 44% yield.

The validity of the structure **13** was established by spectral data as detailed in the experimental section. The mechanism of formation of **13** is considered to be as follows: the spiro 1,3-oxazine **6**, on treatment with base, would be transformed into the 1,3-oxazin-4-one

B. Nucleophilic attack of phenylhydrazine at the 2-position of the 1,3-oxazine would then give an intermediate C, whose cyclization affords the 1,2,4-triazole *C*-nucleoside **13** *via* an

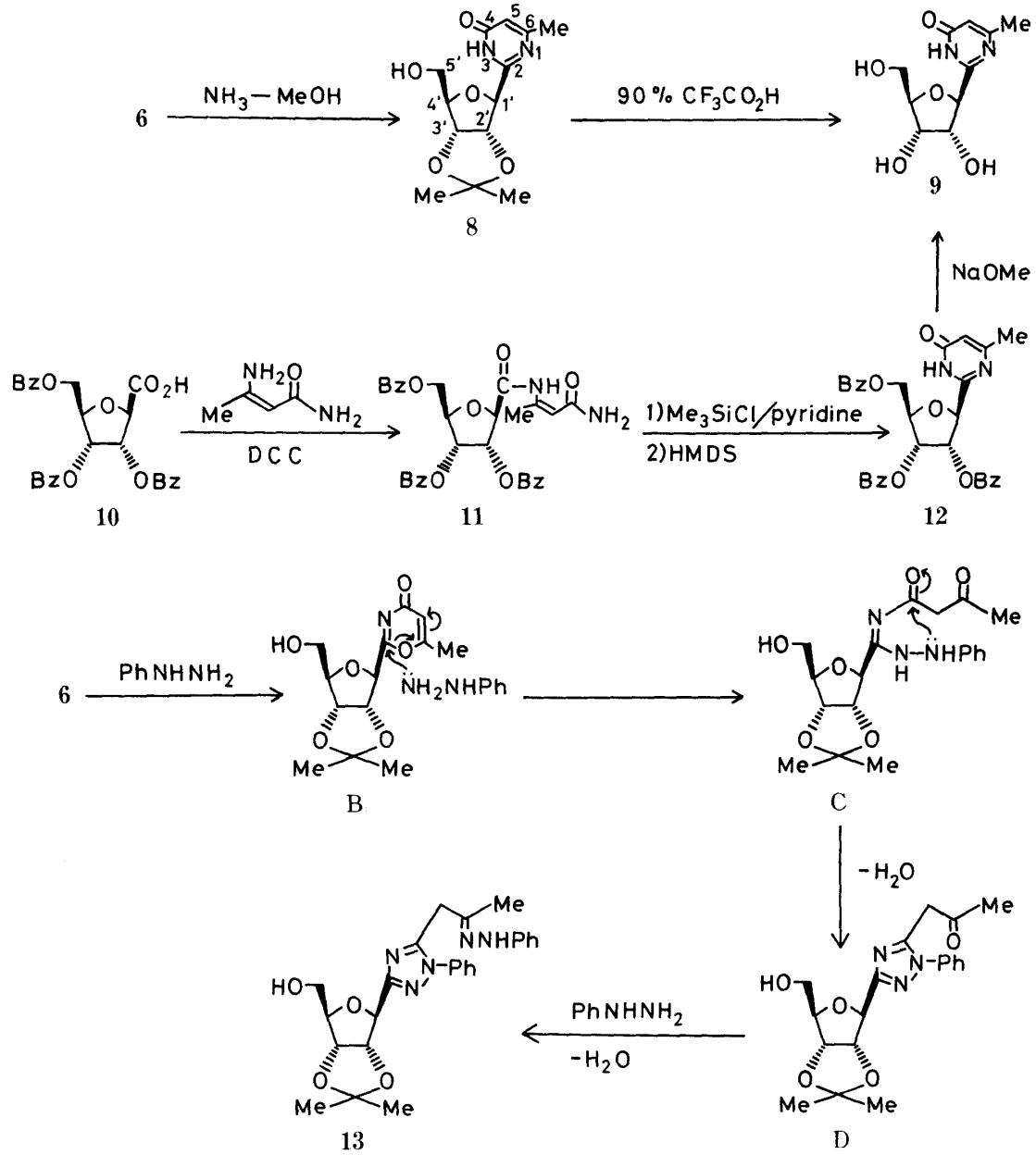

Chart 3

intermediate D. An attempt to deprotect **13** with 90% trifluoroacetic acid was unsuccessful.

Huynh-Dinh and Igolen[15] have demonstrated that the ribofuranosylthioformimidate **14**, prepared by passing hydrogen chloride over a solution of **4** and benzyl hydrosulfide in anhydrous ether, can be used as a key intermediate for the synthesis of *C*-nucleosides. Thus, we investigated the reaction of diketene with **14**. However, treatment of **14** with triethylamine, followed by diketene did not give the desired 1,3-oxazine, but gave compound **4**. Again, we tried to prepare the fully protected D-ribofuranosylthioformimidate **15** from **1** and benzyl hydrosulfide, and to investigate the reaction with diketene. Passage of hydrogen chloride gas over a solution of **1** and benzyl hydrosulfide in anhydrous ether gave the thioformimidate hydrochloride **15** in 95% yield. After treatment of **15** with triethylamine, the resulting free thioformimidate reacted with diketene to give the 1,3-oxazin-4-one **16** in 54% yield. The IR

spectrum of **16** showed the absorption bands characteristic of 1,3-oxazin-4-one at 1690 and 1665 cm^{-1}.[16] In the ^1H-NMR spectrum the signals due to oxazine and dihydrofuran ring protons were observed at δ 6.03 (s) and 6.45 (1H, d, $J=3$ Hz, 3-H), respectively. These spectral data are consistent with the structure of **16** being 2-[4(*S*)-benzoyloxy-5(*R*)-benzoyloxymethyl-4,5-dihydro-2-furyl]-6-methyl-4*H*-1,3-oxazin-4-one.

Since we speculated that **16** could be useful as an intermediate for the synthesis of 2′-deoxy-*C*-nucleosides, which are little known, we investigated the ring transformation of **16** with various nucleophilic reagents. When **16** was allowed to react with ammonia, the desired **17′** was not obtained and 6-methyl-2-(5-hydroxymethyl-2-furyl)pyrimidin-4(3*H*)-one (**17**) was obtained as the sole product in 93% yield. Similarly, the reaction of **16** with hydroxylamine and phenylhydrazine did not give the corresponding dihydrofurans but gave the furan derivatives **18** and **19** in 44 and 59% yields, respectively.

In conclusion, though the yields must be improved, we feel that the present work provides a new methodology for the synthesis of *C*-nucleosides.

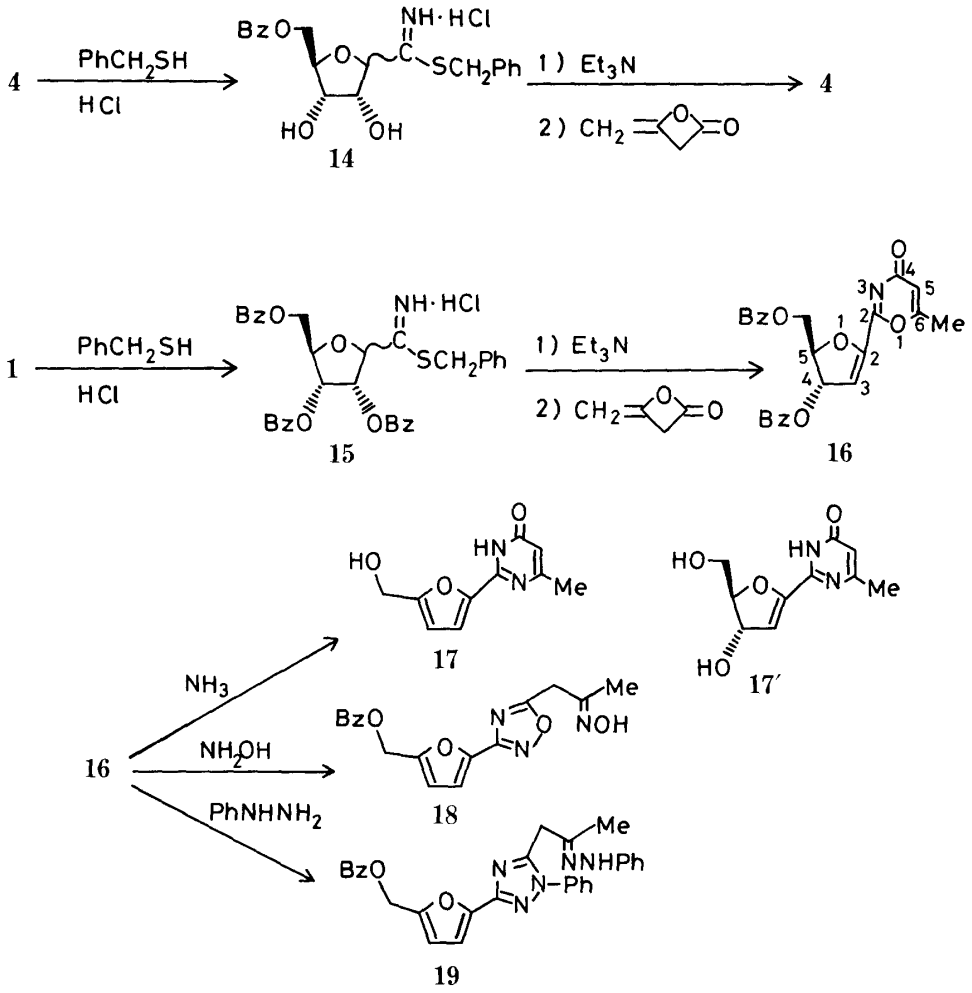

Chart 4

Experimental

Melting points were determined on a Yanaco model MP instrument. ^1H-NMR and ^{13}C-NMR spectra were recorded on a JEOL JNM FX-100 spectrometer using tetramethylsilane as an internal standard. High resolution mass spectra (MS) were taken with a JMS OIS G-2 machine. Wako gel (C-200) was employed for silica gel column chromatography.

***rel*-(1*R*,2*R* or 2*S*,5*R*,6*R*,7*R*)-6,7-(Isopropylidenedioxy)-3,8-dioxabicyclo[3.2.1]octane-2-spiro-2′-(3′,4′-dihydro-6′-methyl-2′*H*-1′,3′-oxazin-4′-one) (6)**——A solution of sodium methoxide in methanol [prepared from NaH (60% oil, 60 mg, 1.5 mmol) and abs. methanol (1 ml)] was added dropwise to a suspension of **5** (1.5 g, 5 mmol) in abs. methanol (5 ml) with stirring. The mixture was stirred for 1 h at room temperature, and then neutralized with ion exchange resin (Amberlite IRC-50). The resin was filtered off, and the filtrate was concentrated *in vacuo*. Methanol was removed by coevaporation with abs. benzene (5 ml) and the residue was dissolved in anhydrous ether (4 ml). Diketene (0.5 g, 6 mmol) was added to the solution, followed by addition of triethylamine (two drops). The mixture was stirred overnight at room temperature. The reaction mixture was concentrated *in vacuo*, and the residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (1 : 2) gave a crystalline substance, which was recrystallized from ethyl acetate to give the product **6**, mp 177—179 °C, colorless prisms, 0.26 g (18%). IR ($CHCl_3$): 3420, 1680 cm^{-1}. *Anal.* Calcd for $C_{13}H_{17}NO_6$: C, 55.12; H, 6.05; N, 4.95. Found: C, 55.13; H, 6.25; N, 5.04.

3,4-*O*-Isopropylidene-2,5-anhydro-D-allonamide (7)——Employing the procedure given for compound **6**, **5** (0.6 g, 2 mmol) was treated with sodium methoxide in abs. methanol at room temperature. The mixture was neutralized with ion exchange resin, and then concentrated *in vacuo*. The residue was subjected to silica gel column chromatography. Elution with ethyl acetate gave a crystalline substance, which was recrystallized from hexane–ethyl acetate to give the product **7**, mp 118—120 °C, colorless needles, 0.3 g (69%). $[\alpha]_D^{20}$ −3.6° (c=6.3, MeOH). IR ($CHCl_3$): 3540, 3440, 1680 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.42 and 1.62 (3H, s, isopropylidene-Me), 3.0—3.5 (3H, br, NH_2 and OH), 3.75 (2H, m, 6-H), 4.23 (1H, m, 5-H), 4.40 (1H, d, J=3 Hz, 2-H), 4.45—5.00 (2H, m, 3,4-H). *Anal.* Calcd for $C_9H_{15}NO_5$: C, 49.76; H, 6.96; N, 6.45. Found: C, 49.61; H, 7.19; N, 6.18.

2-(2′,3′-*O*-Isopropylidene-β-D-ribofuranosyl)-6-methylpyrimidin-4(3*H*)-one (8)——A solution of **6** (0.1 g) in abs. methanol (5 ml) and liq. ammonia (5 ml) was allowed to stand at room temperature in a sealed tube for 6 h. The mixture was concentrated *in vacuo*, and the residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (1 : 2) gave a crystalline substance, which was recrystallized from ethyl acetate to give the product **8**, mp 183 °C, colorless needles, 80 mg (80%). $[\alpha]_D^{20}$ −104° (c=1.5, MeOH). IR ($CHCl_3$): 3300, 1650, 1590 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.36 and 1.61 (3H, s, isopropylidene-Me), 2.32 (3H, s, 6-Me), 3.60—4.15 (2H, m, ABX, 5′-H), 4.18 (1H, m, 4′-H), 4.55—5.00 (3H, m, 1′,2′,3′-H), 6.23 (1H, s, 5-H). ^{13}C-NMR ($CDCl_3$) δ: 24.01 (6-Me), 25.36 and 27.36 (isopropylidene-Me), 61.35 (5′-C), 80.20, 83.66, 85.19, and 86.24 (1′,2′,3′,4′-C), 111.25 (5-C), 115.54 (isopropylidene-C), 158.69, 165.26, and 167.26 (2,4,6-C). *Anal.* Calcd for $C_{13}H_{18}N_2O_5$: C, 55.31; H, 6.43; N, 9.92. Found: C, 55.09; H, 6.47; N, 9.81.

2-(β-D-Ribofuranosyl)-6-methylpyrimidin-4(3*H*)-one (9)——1) A solution of **8** (70 mg) in 90% trifluoroacetic acid (2 ml) was allowed to stand at room temperature for 1 h. The solvent was coevaporated with benzene and ethanol *in vacuo*, and the residue was washed with ether. The resulting residue was dissolved in abs. methanol. The solvent was removed *in vacuo* to give a crystalline substance, which was recrystallized from ethyl acetate–abs. methanol to yield the product **9**, mp 187 °C, colorless needles, 50 mg (83%). IR (KBr): 3350, 1685, 1605 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.27 (3H, s, 6-Me), 3.60—4.25 (5H, m, 2′,3′,4′,5′-H), 4.69 (1H, d, J=3 Hz, 1′-H), 6.12 (1H, s, 5-H). *Anal.* Calcd for $C_{10}H_{14}N_2O_5$: C, 49.58; H, 5.83; N, 11.57. Found: C, 49.36; H, 5.88; N, 11.30.

2) A solution of sodium methoxide in methanol [prepared from NaH (60% oil, 40 mg, 1 mmol) and abs. methanol (1 ml)] was added to a solution of **12** (120 mg, 0.2 mmol) in abs. methanol (2 ml) with ice-cooling. The mixture was stirred at room temperature for 20 min, and neutralized with ion exchange resin (Amberlite IRC-50). The solvent was evaporated off *in vacuo*, and the residue was washed with anhydrous ether. The resulting crystals were recrystallized from ethyl acetate–abs. methanol to give the product **9**, 40 mg (83%).

3-(3,4,6-Tri-*O*-benzoyl-2,5-anhydro-D-allonamido)crotonamide (11)——A solution of DCC (0.88 g, 4 mmol) in chloroform (5 ml) was added dropwise to a solution of 3-aminocrotonamide (0.21 g, 2.1 mmol) and 3,4,6-tri-*O*-benzoyl-2,5-anhydro-D-allonic acid (**10**) (0.5 g, 1 mmol) in chloroform (5 ml) with stirring and ice-cooling. The mixture was stirred at room temperature for 3 h. The precipitated crystals were filtered off, and the filtrate was concentrated *in vacuo*. The residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (3 : 1) gave the product **11** as an amorphous powder, 0.35 g (60%). IR ($CHCl_3$): 3525, 3420, 1720, 1653, 1623 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.28 (3H, s, Me), 4.6—4.8 (5H, m, 2′,5′,6′-H and olefinic-H), 5.5—6.1 (4H, m, NH_2 and 3′,4′-H), 7.2—8.1 (15H, m, benzoyl-H), 12.77 (1H, s, CONH). *Anal.* Calcd for $C_{31}H_{28}N_2O_9 \cdot CH_3CO_2CH_2CH_3$: C, 63.88; H, 5.39; N, 4.36. Found: C, 64.07; H, 5.19; N, 4.13.

2-(2′,3′,5′-Tri-*O*-benzoyl-β-D-ribofuranosyl)-6-methylpyrimidin-4(3*H*)-one (12)——A solution of **11** (120 mg, 0.21 mmol) and trimethylsilyl chloride (50 mg, 0.42 mmol) in dry pyridine (0.9 ml) was stirred for 30 min at room temperature. HMDS (72 mg, 0.42 mmol) was added to the mixture, and then the solution was heated at 75—80 °C for 8 h. The reaction mixture was concentrated *in vacuo*, and the residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (1 : 1) gave the product **12** as an amorphous powder, 110 mg (96%). IR ($CHCl_3$): 3370, 1730, 1680, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.20 (3H, s, 6-Me), 5.13 (1H, d, J=4.4 Hz, 1′-H), 6.13 (1H, s, 5-H). *Anal.* Calcd for $C_{31}H_{26}N_2O_8 \cdot 3/5H_2O$: C, 65.86; H, 4.85; N, 4.95. Found: C, 65.78; H, 4.97; N, 4.83.

5-[3-(2′,3′-*O*-Isopropylidene-β-D-ribofuranosyl)-1-phenyl-1*H*-1,2,4-triazolyl]acetone Phenylhydrazone (13)——A solution of **6** (190 mg, 0.67 mmol) and phenylhydrazine (145 mg, 1.34 mmol) in abs. ethanol (5 ml) was heated under

reflux for 2 h. The mixture was concentrated *in vacuo*, and the residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (1 : 1) gave the product **13** as an amorphous powder, 135 mg (44%). IR ($CHCl_3$): 3360, 3280, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.35, 1.59 (3H, s, isopropylidene-Me), 1.95 (3H, s, Me), 3.79 (2H, s, C–C$\underline{H}_2$–C), 3.61 (1H, dd, J=12, 3.5 Hz, 5′-H), 3.90 (1H, dd, J=12, 3 Hz, 5′-H), 4.47 (1H, m, 4′-H), 4.95 (2H, d, J=1.5 Hz, 2′,3′-H), 5.23 (1H, d, J=1.5 Hz, 1′-H), 6.70—7.70 (10H, m). High resolution MS *m/z*: M^+ Calcd for $C_{25}H_{29}N_5O_4$: 463.2218. Found: 463.2213.

Benzyl 2,3,5-Tri-*O*-benzoyl-D-ribofuranosylthioformimidate Hydrochloride (15)——A solution of **1**[11,17] (4.7 g, 10 mmol) and benzyl hydrosulfide (2.48 g, 20 mmol) in anhydrous ether (200 ml) was saturated with dry hydrogen chloride under ice-cooling. The mixture was allowed to stand at 4 °C for 16 h. The precipitates **15** were collected by suction. mp 82—86 °C, 6.01 g (95%). $[\alpha]_D^{21}$ +4.6° (c=3.0, MeOH). *Anal.* Calcd for $C_{34}H_{30}ClNO_7S$: C, 64.60; H, 4.78; N, 2.22; Cl, 5.61; S, 5.07. Found: C, 64.93; H, 5.09; N, 1.92; Cl, 5.87; S, 5.53.

2-[4(*S*)-Benzoyloxy-5(*R*)-benzoyloxymethyl-4,5-dihydro-2-furyl]-6-methyl-4*H*-1,3-oxazin-4-one (16)——A solution of triethylamine (0.61 g, 6 mmol) in dry benzene (2 ml) was added dropwise to a suspension of **15** (3.16 g, 5 mmol) in dry benzene (50 ml) with stirring. The mixture was stirred at room temperature for 15 min, then anhydrous ether (50 ml) was added. The precipitated triethylamine hydrochloride was filtered off, and the filtrate was concentrated *in vacuo*. The residue was dissolved in anhydrous ether (10 ml). A solution of diketene (0.63 g, 7.5 mmol) in anhydrous ether (2 ml) was added to the above solution followed by addition of triethylamine (two drops). The mixture was refluxed on a water bath for 2 h. The precipitated crystals were collected by suction. The filtrate was concentrated *in vacuo* and the residue was dissolved in benzene. The solution was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (1 : 1) gave a crystalline substance, which was combined with the crystals obtained above, and recrystallized from benzene to give the product **16**, mp 153—154 °C, colorless needles, 1.17 g (54%). $[\alpha]_D^{20}$ +184° (c=1.0, $CHCl_3$). IR ($CHCl_3$): 1720, 1690, 1665, 1635 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.25 (3H, s, Me), 4.65 (2H, d, J=4 Hz, OC$\underline{H}_2$), 5.13 (1H, dt, J=3, 4 Hz, 5-H), 6.03 (1H, s, oxazine 5-H), 6.15 (1H, dd, J=3, 3 Hz, 4-H), 6.45 (1H, d, J=3 Hz, 3-H), 7.2—7.6 (6H, m, benzoyl-H), 7.8—8.1 (4H, m, benzoyl-H). *Anal.* Calcd for $C_{24}H_{19}NO_7$: C, 66.51; H, 4.42; N, 3.23. Found: C, 66.67; H, 4.59; N, 3.07.

6-Methyl-2-(5-hydroxymethyl-2-furyl)pyrimidin-4(3*H*)-one (17)——A solution of **16** (433 mg, 1 mmol) in liq. ammonia (10 ml) was allowed to stand in a sealed tube at −10——5 °C for 2 h, and then at room temperature for 2 h. Excess ammonia was evaporated off, and the residue was washed with ether. The ether-insoluble material was subjected to silica gel column chromatography. Elution with ethyl acetate gave a crystalline substance, which was recrystallized from ethanol to give the product **17**, mp 250—251 °C, colorless needles, 190 mg (93%). IR (KBr): 3350, 1680 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.22 (3H, s, Me), 4.47 (2H, s, –CH_2–), 6.05 (1H, s, pyrimidine 5-H), 6.44 (1H, d, J=4 Hz, furan 4-H), 7.42 (1H, d, J=4 Hz, furan 3-H). *Anal.* Calcd for $C_{10}H_{10}N_2O_3$: C, 58.25; H, 4.89; N, 13.58. Found: C, 58.19; H, 4.85; N, 13.68.

5-[3-(5-Benzoyloxymethyl-2-furyl)-1,2,4-oxadiazolyl]acetone Oxime (18)——A solution of **16** (348 mg, 0.8 mmol) and hydroxylamine–abs. methanol (4 ml, 0.5 mmol/ml) was stirred at room temperature for 6 h. The mixture was concentrated *in vacuo*, and the residue was subjected to silica gel column chromatography. Elution with hexane–ethyl acetate (3 : 1) gave a crystalline substance (120 mg, 44%), which was recrystallized from hexane–ether to give the product **18**, mp 119—121 °C, colorless needles. IR (KBr): 3580, 3220, 1720, 1622, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.05 (3H, s, Me), 3.90 (2H, s, C–C$\underline{H}_2$–C), 5.43 (2H, s, OC$\underline{H}_2$), 6.25 (1H, br, OH), 6.70 (1H, d, J=6 Hz, furan 4-H), 7.19 (1H, d, J=6 Hz, furan 3-H), 7.3—7.7 (3H, m, benzoyl-H), 8.0—8.3 (2H, m, benzoyl-H). *Anal.* Calcd for $C_{17}H_{15}N_3O_5$: C, 59.82; H, 4.43; N, 12.31. Found: C, 59.80; H, 4.53; N, 12.24.

5-[3-(5-Benzoyloxymethyl-2-furyl)-1-phenyl-1*H*-1,2,4-triazolyl]acetone Phenylhydrazone (19)——A solution of **16** (87 mg, 0.2 mmol) and phenylhydrazine (43 mg, 0.4 mmol) in abs. ethanol (2 ml) was refluxed on a water bath for 30 min. The mixture was concentrated *in vacuo* to give an oily residue, to which chloroform was added. The separated crystals (60 mg, 59%) were collected by suction. Recrystallization from chloroform gave the product **19**, mp 206—207 °C, pale yellow prisms. IR (KBr): 3240, 1718 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.96 (3H, s, Me), 3.89 (2H, s, C–C$\underline{H}_2$–C), 5.36 (2H, s, OCH_2–), 6.60 (1H, d, J=3 Hz, furan 4-H), 6.67—7.65 (13H, m, phenyl-H and benzoyl-H), 7.50 (1H, d, J=3 Hz, furan 3-H), 7.95—8.05 (2H, m, benzoyl-H). *Anal.* Calcd for $C_{29}H_{25}N_5O_3 \cdot H_2O$: C, 68.35; H, 5.34; N, 13.75. Found: C, 68.21; H, 4.88; N, 13.55.

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