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Synthesis and anti-HIV activity of L-β-3′-*C*-cyano-2′,3′-unsaturated nucleosides and L-3′-*C*-cyano-3′-deoxyribonucleosides

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Abstract—An efficient synthetic method was developed for L-β-3′-*C*-cyano-2′,3′-unsaturated nucleosides and L-3′-*C*-cyano-3′-deoxyribonucleosides. The key intermediate **11** was obtained from L-xylose, from which a series of pyrimidine and purine nucleosides were prepared in high yield by the coupling of **11** and various silyl-protected bases in the presence of TMSOTf. These nucleosides were eliminated, followed by deprotecting to give L-β-3′-*C*-cyano-2′,3′-unsaturated nucleosides. When selectively deprotected by hydrazine hydrate in buffered acetic acid–pyridine followed by treatment with potassium carbonate in methanol, L-3′-*C*-cyano-3′-deoxyribonucleosides were obtained. The synthesized nucleosides were tested for anti-HIV activity.

1. Introduction

Nucleoside analogs are used extensively as chemotherapeutic agents targeting human immunodeficiency virus (HIV), the virus responsible for acquired immunodeficiency syndrome (AIDS). The past decade has witnessed the discovery of a class of 2′,3′-unsaturated nucleosides such as d4T,[1] L-d4C,[2] L-d4FC[2] and abacavir[3] as interesting therapeutic agents against HIV. As part of our efforts to develop novel antiviral agents, we recently reported the synthesis and anti-HIV activity of L-β-2′(or 3′)-fluoro-2′,3′-unsaturated nucleosides[4] and L-β-2′(or 3′)-fluoro-2′,3′-unsaturated 4′-thionucleosides.[5] These nucleosides were designed to take advantage of the characteristics of L-nucleosides, particularly the lower toxicity that they showed in many instances compared to their D-counterparts.[4–6] In view of the interesting biological activity of these compounds, we decided to extend our studies to L-3′-*C*-cyano-2′,3′-didehydro-3′-dideoxynucleosides (L-3′-*C*-cyano-d4Ns), in which an electronegative cyano group replaces the fluorine atom. Previously, the synthesis of D-3′-*C*-cyano-d4Ns via elimination reaction started from individual D-nucleosides.[7] Such a linear approach involves the repetition of the same scheme for each nucleoside. Besides, the synthesis of L-isomers is complicated by the unavailability of L-nucleosides as starting materials. For these reasons, we developed an efficient synthetic route in which a common key intermediate can be coupled to different heterocyclic moieties to obtain a series of L-3′-*C*-cyano-d4Ns. Our scheme also afforded another interesting class of nucleosides: L-3′-*C*-cyano-3′-deoxyribonucleosides from the key intermediates. Both types of nucleosides were evaluated for anti-HIV activity.

2. Results and discussion

2.1. Chemistry

Compound **11** was the key intermediate in our synthesis. As earlier described for the synthesis of the D-enantiomer,[7,8] Protected L-xylose **1**[9] was converted to 3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-α-L-ribo-pentofura-nose **8** in 63% overall yield (Scheme 1). Benzoylation of the 5-hydroxyl group gave compound **9**, which was deprotected to a lactol **10** by using 90% trifluoroacetic acid.

Acetylation of **10** afforded the key intermediate **11** as an epimeric mixture. Condensation of **11** with various silylated pyrimidines gave the corresponding pyrimidine analogs **12**–**14** in 80–86% yield (Scheme 2). The condensation reaction gave the β-anomer by virtue of the neighbor group participating effect of the 2-acetyl group. With the aid of the acidic 3′-α proton[10] accompanied by a good leaving group (OAc) at the 2′ position, compounds **12**–**14** were quantitatively converted to 2′,3′-unsaturated compounds **18**–**20** by treatment with DBU (0.2 equiv.)/DMAP (6 equiv.) in dichloromethane. Compounds **18** and **19** could be directly

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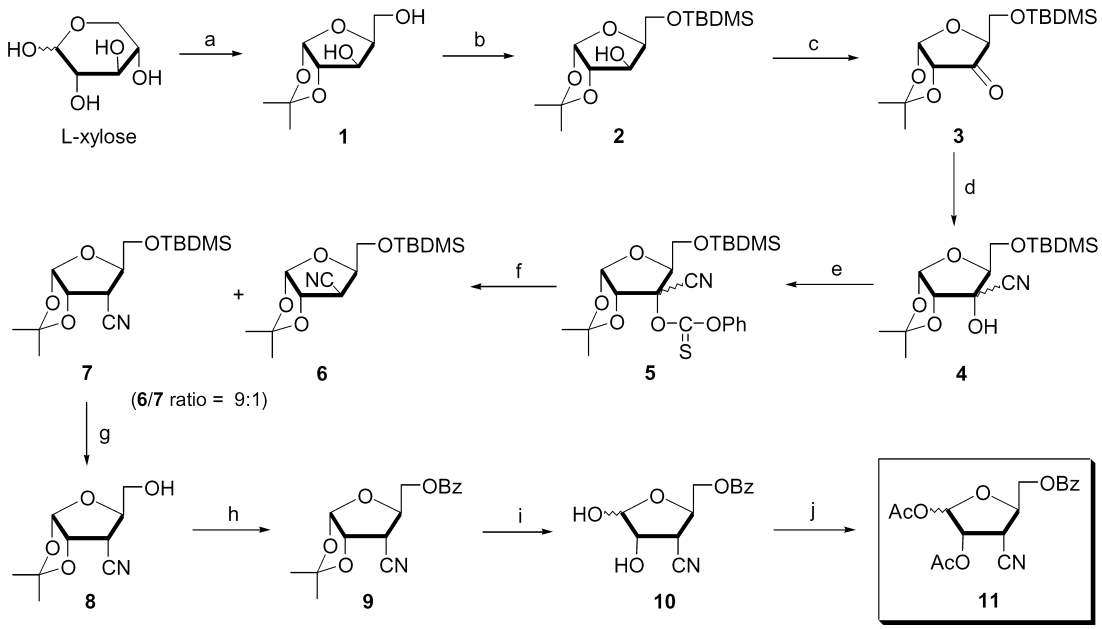
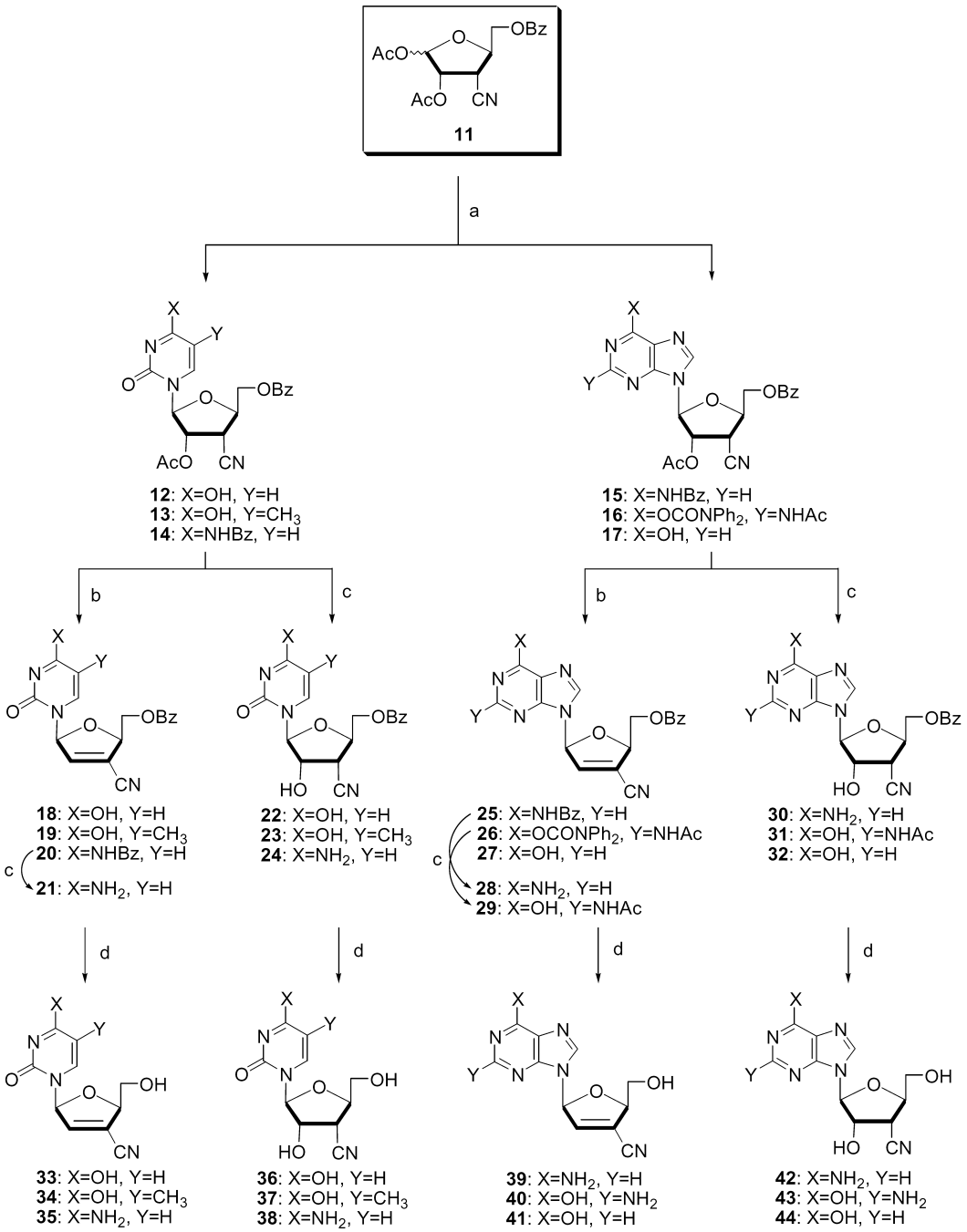


Scheme 1. (a) (i) H_2SO_4, $CuSO_4$, acetone, rt; (ii) 0.2% HCl solution, rt; (b) TBDMSCl, imidazole, CH_2Cl_2, rt; (c) PCC, Ac_2O, 4 Å M. S., CH_2Cl_2, rt; (d) NaCN, $NaHCO_3$, H_2O, Et_2O, rt; (e) PhOC(S)Cl, DMAP, CH_2Cl_2, rt; (f) AIBN, Bu_3SnH, toluene, 80–90°C; (g) 0.1N HCl, MeOH; (h) BzCl, Py/CH_2Cl_2; (i) TFA, H_2O; (j) Ac_2O, Py.

deprotected by careful treatment with a catalytic amount of potassium carbonate in methanol in 20 min to give the desired L-β-3′-*C*-cyano-2′,3′-unsaturated uracil derivative **33** and L-β-3′-*C*-cyano-2′,3′-unsaturated thymine derivative **34** in ca. 70% yield. Compound **20** could not be converted to the desired compound **35** when using the same procedure described for **18** and **19**. Our understanding is that longer time required for the deprotection of the benzamidic functionality in compound **20** allows the competitive deprotonation of H-4′, with elimination of the base and formation of a furan-type product. As further evidence of this mechanism, when **18** and **19** were treated with potassium carbonate in methanol for more than 1 h, the yields for **33** and **34** were very low, about 8–10%, and a similar decomposition pattern was observed. When compounds **18**–**20** were tested for acid–base stability, their half-life at pH 11.0 was found to be only 2 h, whereas the compounds were stable at pH 2.0 and 7.0. Because of the lability of these nucleosides under basic conditions, the deprotection reaction for **20** was run in two steps. First, selective N^4-debenzoylation was accomplished using hydrazine hydrate in buffered acetic acid–pyridine[11] to give **21**. Compound **21** was then treated with potassium carbonate in methanol under carefully controlled conditions to afford compound **35**. The total yield for the two steps was about 60%. This two-step deprotection strategy was also applied for the formation of L-β-3′-*C*-cyano-3′-deoxy–ribonucleosides **36**–**38** (Scheme 2). Because of the acidity of 3′-H and the presence of a leaving group at the 2′-position, attempts to deprotect **12**–**14** by potassium carbonate in methanol or NH_3/MeOH did not produce the desired products. Instead, complex mixtures were obtained, containing also β-elimination products. Removal of the 2′-acetyl group by treatment with hydrazine hydrate in buffered acetic acid–pyridine to selectively deprotect 2′-OAc to 2′-OH allowed us to remove the leaving group, thereby avoiding the elimination reaction under the subsequent basic conditions. As a result, compounds **22**–**24** could be deprotected by treatment with potassium carbonate in methanol to produce the desired products **36**–**38** in good yields. For the synthesis of purine analogs, the key intermediate **11** was condensed with silylated N^6-benzoyladenine and N^2-acetyl-6-*O*-diphenylcarbamoylguanine derivatives to give the corresponding nucleosides **15** and **16** in 75 and 62% yields, respectively (Scheme 2). In both cases, only N-9 glycosylation products were obtained. However, when **11** was condensed with silylated hypoxanthine, besides the N-9 isomer **17**, also the N-7 isomer was obtained, with a N-9/N-7 ratio of 5:1 in 73% total yield. The pure compound **17** was isolated from the mixture by recrystallization from methanol/acetone/hexane. The unsaturated purines **25**–**27** were obtained by using the same elimination procedure as described for the pyrimidines **12**–**14** with DBU/DMAP. Nucleosides **25** and **26** were deprotected by treatment with hydrazine hydrate in buffered acetic acid–pyridine to give **28** and **29**, respectively. In the latter compound, the N^2-acetate could not be deprotected under the reaction conditions. This caused the final deprotection step to **40** to proceed in lower yield (35%) than for the deprotection of **27** to **41** (65%) and **28** to **39** (71%). By using the same procedure employed for pyrimidines **36**–**38**, purines **15**–**17** were first selectively deprotected by hydrazine hydrate in buffered acetic acid–pyridine, then further deprotected by treatment with potassium carbonate in methanol to give L-3′-*C*-cyano-3′-deoxyribonucleosides **42**–**44**.

2.2. Anti-HIV activity

The synthesized L-β-3′-*C*-cyano-2′,3′-unsaturated nucleosides (**33**–**35**, **39**–**41**) and L-3′-*C*-cyano-3′-deoxyribonucleosides (**36**–**38**, **42**–**44**) were evaluated against HIV-1 in human PBM cells in vitro and the results are summarized in Tables 1 and 2. Among the tested nucleosides, only compounds **33** (EC_{50} 21.7 μM), **34** (EC_{50} 38.0 μM), **39** (EC_{50} 67.4 μM), **40** (EC_{50} 28.0 μM) and **42**



Scheme 2. (a) BSA, pyrimidines or purines, TMSOTf, CH_3CN; (b) DMAP, DBU, CH_2Cl_2; (c) $N_2H_4{\cdot}H_2O$, AcOH, Py; (d) K_2CO_3, MeOH.

(EC_{50} 74.8 μM) showed modest anti-HIV activity. Only the guanosine analog showed some cytotoxicity (IC_{50} 46.7 μM).

3. Conclusion

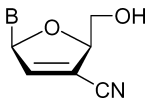
We described an efficient and convenient route for the synthesis of L-β-3′-*C*-cyano-2′,3′-didehydro-2′3′-dideoxy-nucleosides and L-β-3′-*C*-cyano-3′-deoxyribonucleosides. Our scheme features a convergent approach in which the common key intermediate can be coupled to an array of heterocycles to synthesize a series of modified nucleosides, thus overcoming the limitation of linear approaches previously reported for the synthesis of D-isomers.[7] The newly synthesized compounds were evaluated for anti-HIV activity and four of them showed modest antiviral activity.

4. Experimental

4.1. General

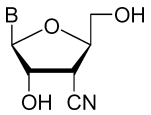
Melting points were determined on a Mel-temp II apparatus and are uncorrected. Nuclear magnetic resonance spectra were recorded on a Bruker 400 AMX spectrometer at 400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR with tetramethylsilane as the internal standard. Chemical shifts

Table 1. Anti-HIV activity and cytotoxicity of L-3′-*C*-cyano-2′,3′-unsaturated nucleosides



Compd (B)	HIV (EC_{50}, μM)	Toxicity (IC_{50}, μM)		
	PBM	PBM	CEM	VERO
33 (Uracil)	21.7	>100	>100	>100
34 (Thymine)	38.0	>100	82.9	>100
35 (Cytosine)	>100	>100	>100	>100
39 (Adenine)	67.4	>100	>100	>100
40 (Guanine)	28.0	>100	46.7	>100
41 (Hypoxanthine)	50.0	>100	>100	>100
AZT	0.004	>100	14.3	29.0

Table 2. Anti-HIV activity and cytotoxicity of L-3′-*C*-cyano-2′,3′-unsaturated nucleosides



Compd (B)	HIV (EC_{50}, μM)	Toxicity (IC_{50}, μM)		
	PBM	PBM	CEM	VERO
36 (Uracil)	>100	>100	>100	>100
37 (Thymine)	>100	>100	>100	>100
38 (Cytosine)	>100	>100	>100	>100
42 (Adenine)	74.8	>100	>100	>100
43 (Guanine)	>100	>100	>100	>100
44 (Hypoxanthine)	>100	>100	>100	>100
AZT	0.004	>100	14.3	29.0

(δ) are reported in parts per million (ppm), and signals are reported as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br (broad singlet). UV spectra were recorded on a Beckman DU-650 spectrophotometer. Optical rotations were measured on a Jasco DIP-370 digital polarimeter. Mass spectra were recorded on a Micromass Autospec high-resolution mass spectrometer. TLC was performed on Uniplates (silica gel) purchased from Analtech Co. Column chromatograph was performed using silica gel G (TLC grade, >440 mesh) for vacuum flash column chromatograph. Elemental analyses were performed by Atlantic Microlab Inc., Norcross, GA.

4.1.1. 5-*O*-Benzoyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-α-L-ribofuranose (9). To a solution of 3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-α-L-ribofuranose (**8**)[7–9] (20 g, 0.1 mol) and pyridine (16 mL, 0.2 mol) in dry dichloromethane (300 mL), benzoyl chloride (14 mL, 0.12 mol) was added dropwise at 0°C with stirring. The mixture was stirred for 1 h at rt with the exclusion of moisture. Water (100 mL) was added, and stirred for 10 min more. After separation, the organic phase was subsequently washed with 1% HCl (100 mL), saturated sodium bicarbonate (100 mL) and brine (100 mL), dried over sodium sulfate, filtered and concentrated. The residue was purified by silica gel column chromatography (hexane/ethyl acetate, 10:1–3:1) to give compound **9** (28.8 g, 95% yield) as a white solid: R_f 0.58 (hexane/ethyl acetate, 2:1); mp 95–97°C; $[\alpha]_D^{25}=-96.8$ (*c* 2.9, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 8.07–7.43 (m, 5H), 5.93 (d, *J*=3.5 Hz, 1H), 4.89 (t, *J*=4.1 Hz, 1H), 4.63–4.54 (m, 3H), 2.99 (dd, *J*=9.4, 4.5 Hz, 1H), 1.61 (s, 3H), 1.37 (s, 3H); MS (ESI) *m*/*z* 304 (MH^+). Anal. calcd for $C_{16}H_{17}NO_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.32; H, 5.54; N, 4.57.

4.1.2. 1,2-Di-*O*-acetyl-5-*O*-benzoyl-3-*C*-cyano-3-deoxy-L-ribofuranose (11). A solution of **9** (28 g, 92.0 mmol) in trifluoroacetic acid/water (30 mL, 9:1 v/v) was stirred for 6 h. The mixture was concentrated in vacuum to crude **10**. This was diluted with dry pyridine (40 mL). After cooling to 0°C, acetic anhydride (23 mL, 240 mmol) was added dropwise with stirring at 0–8°C, and stirring was continued for 12 h at rt. The mixture was concentrated in vacuum, diluted with dichloromethane (200 mL), washed with aqueous 5% sodium bicarbonate (100 mL) and water (100 mL), dried over sodium sulfate, filtered and concentrated. The residue was purified by silica gel column chromatography (hexane/ethyl acetate, 10:1–3:1) to give the pure anomeric mixture **11** (32 g, 90% yield) as a white solid: R_f 0.50 (hexane/ethyl acetate, 2:1); ^{1}H NMR ($CDCl_3$) δ 8.08–7.45 (m, 5H), 6.49 and 6.20 (d and s, *J*=4.1 Hz, 1H), 5.47 and 5.30 (d and dd, *J*=4.6 Hz; 8.8, 4.2 Hz, 1H), 4.85–4.46 (m, 3H), 3.66–3.54 (m, 1H), 2.22 and 2.20 (2×s, 3H), 1.90 (s, 3H); MS (ESI) *m*/*z* 348 (MH^+). Anal. calcd for $C_{17}H_{17}NO_7$: C, 58.79; H, 4.93; N, 4.03. Found: C, 58.60; H, 4.97; N, 4.03.

4.1.3. 1-(2′-*O*-Acetyl-5′-*O*-benzoyl-3′-*C*-cyano-3′-deoxy-L-ribofuranosyl)uracil (12). *N*,*O*-Bis(trimethylsilyl)acetamide (BSA, 4.4 mL, 18 mmol) was added at rt to a mixture of compound **11** (2.10 g, 6.0 mmol) and uracil (800 mg, 7.2 mmol) in anhydrous acetonitrile (40 mL), then stirred under argon for 2 h at 50–60°C to form a clear solution. After being cooled to rt, trimethylsilyl trifluoromethanesulfonate (TMSOTf, 1.2 mL, 6.6 mmol) was added, and the resulting mixture was refluxed for 10 h under argon. The reaction mixture was cooled to rt, then quenched with saturated aqueous sodium bicarbonate solution (20 mL) and stirred until the evolution of CO_2 ceased. The resulting mixture was diluted with ethyl acetate (150 mL), washed with brine (2×100 mL), dried over sodium sulfate, filtered and concentrated. The residue was purified by silica gel column chromatography (dichloromethane/methanol, 50:1) to give compound **12** (2.0 g, 84% yield) as a white foam: R_f 0.63 (CH_2Cl_2/MeOH, 10:1); $[\alpha]_D^{25}=-3.8$ (*c* 0.35, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 8.78 (br, 1H), 8.08–7.45 (m, 5H), 7.14 (d, *J*=8.1 Hz, 1H), 5.73 (dd, *J*=6.4, 1.5 Hz, 1H), 5.68 (d, *J*=8.1 Hz, 1H), 5.34 (d, *J*=1.5 Hz, 1H), 4.72 (dd, *J*=11.8, 3.7 Hz, 1H), 4.66 (dt, *J*=10.0, 3.9 Hz, 1H), 4.59 (dd, *J*=11.8, 4.0 Hz, 1H), 4.08 (dd, *J*=10.0, 6.4 Hz, 1H), 2.25 (s, 3H); MS (ESI) *m*/*z* 400 (MH^+). Anal. calcd for $C_{19}H_{17}N_3O_7{\cdot}0.2H_2O$: C, 56.63; H, 4.35; N, 10.43. Found: C, 56.60; H, 4.38; N, 10.27.

4.1.4. 1-(2′-*O*-Acetyl-5′-*O*-benzoyl-3′-*C*-cyano-3′-deoxy-L-ribofuranosyl)thymine (13). Using the same procedure as described for **12**, compound **11** (2.10 g, 6.0 mmol) was condensed with thymine (900 mg, 7.2 mmol) for 10 h to produce compound **13** (2.13 g, 86% yield) as a white foam: R_f 0.68 (CH_2Cl_2/MeOH, 10:1); $[\alpha]_D^{24}=+11.1$ (*c* 0.6,

CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 8.49 (br, 1H), 8.08–7.44 (m, 5H), 6.93 (s, 1H), 5.73 (dd, J=6.4, 1.4 Hz, 1H), 5.34 (d, J=1.4 Hz, 1H), 4.73 (dd, J=12.0, 3.7 Hz, 1H), 4.64 (dt, J=10.0, 3.9 Hz, 1H), 4.57 (dd, J=12.0, 3.9 Hz, 1H), 4.12 (dd, J=10.0, 6.4 Hz, 1H), 2.25 (s, 3H), 1.83 (s, 3H); MS (ESI) m/z 414 (MH^+). Anal. calcd for $C_{20}H_{19}N_3O_7 \cdot 0.3H_2O$: C, 57.36; H, 4.72; N, 10.03. Found: C, 57.32; H, 4.67; N, 9.80.

4.1.5. 1-(2′-*O*-Acetyl-5′-*O*-benzoyl-3′-*C*-cyano-3′-deoxy-L-ribofuranosyl)-*N*^{4}-benzoylcytosine (14). Using the same procedure as described for **12**, compound **11** (2.10 g, 6.0 mmol) was condensed with N^4-benzoyl cytosine (1.55 g, 7.2 mmol) for 10 h to produce compound **14** (2.41 g, 80% yield) as a white foam: R_f 0.62 (CH_2Cl_2/MeOH, 20:1); $[\alpha]_D^{23}=-20.0$ (c 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 9.05 (br, 1H), 8.09–7.45 (m, 12H), 5.96 (d, J=6.0 Hz, 1H), 5.59 (s, 1H), 4.78–4.66 (m, 3H), 4.12 (dd, J=10.4, 6.0 Hz, 1H), 2.20 (s, 3H); MS (ESI) m/z 503 (MH^+). Anal. calcd for $C_{26}H_{22}N_4O_7$: C, 62.15; H, 4.41; N, 11.15. Found: C, 61.85; H, 4.27; N, 11.13.

4.1.6. *N*^{6}-Benzoyl-9-(2′-*O*-acetyl-5′-*O*-benzoyl-3′-*C*-cyano-3′-deoxy-L-ribofuranosyl)adenine (15). Using the same procedure as described for **12**, compound **11** (2.10 g, 6.0 mmol) was condensed with N^6-benzoyl adenine (1.72 g, 7.2 mmol) for 24 h to produce compound **15** (2.40 g, 75% yield) as a white foam: R_f 0.72 (CH_2Cl_2/MeOH, 10:1); $[\alpha]_D^{22}=+8.5$ (c 1, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 8.95 (br, 1H), 8.60 (s, 1H), 8.02 (s, 1H), 8.00–7.39 (m, 10H), 6.09 (d, J=4.5 Hz, 1H), 6.02 (s, 1H), 4.83–4.76 (m, 3H), 4.63 (m, 1H), 2.28 (s, 3H); MS (ESI) m/z 527 (MH^+). Anal. calcd for $C_{27}H_{22}N_6O_6 \cdot 0.4MeOH$: C, 61.02; H, 4.41; N, 15.58. Found: C, 61.21; H, 4.57; N, 15.32.

4.1.7. *N*^{2}-Acetyl-6-*O*-diphenylcarbamoyl-9-(2′-*O*-acetyl-5′-*O*-benzoyl-3′-*C*-cyano-3′-deoxy-L-ribofuranosyl)-guanine (16). Using the same procedure as described for **12**, compound **11** (4 g, 11.5 mmol) was condensed with N^2-acetyl-6-*O*-diphenylcarbamoyl guanine[12] (5.36 g, 13.8 mmol) for 24 h to produce compound **16** (4.82 g, 62% yield) as a white foam: R_f 0.3 (hexane/ethyl acetate, 1:1); $[\alpha]_D^{25}=-7.6$ (c 0.68, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 8.23 (br, 1H), 7.91–7.32 (m, 16H), 5.90 (s, 1H), 5.88 (d, J=5.9 Hz, 1H), 5.69 (m, 1H), 4.80 (dt, J=10.3, 4.9 Hz, 1H), 4.68 (dd, J=12.0, 4.3 Hz, 1H), 4.63 (dd, J=12.0, 5.3 Hz, 1H), 2.22 (s, 3H), 2.12 (s, 3H); MS (ESI) m/z 676 (MH^+), 698 (M+Na). Anal. calcd for $C_{35}H_{29}N_7O_8$: C, 62.22; H, 4.33; N, 14.51. Found: C, 62.57; H, 4.18; N, 14.37.

4.1.8. 9-(2′-*O*-acetyl-5′-*O*-benzoyl-3′-*C*-cyano-3′-deoxy-L-ribofuranosyl)hypoxanthine (17). Using the same procedure as described for **12**, compound **11** (3 g, 8.6 mmol) was condensed with hypoxanthine (1.76 g, 13 mmol) for 36 h to produce compound **17** (2.22 g, 61% yield) accompanied with its N-7 isomer (0.44 g, 12% yield). The pure N-9 isomer was recrystallized from the mixture in methanol/acetone/hexanes: R_f 0.45 (CH_2Cl_2/MeOH, 10:1); mp 248–250°C; ^1H NMR (DMSO-d_6) δ 12.43 (br, 1H), 8.22 (s, 1H), 7.92 (s, 1H), 7.91–7.47 (m, 5H), 6.29 (d, J=1.6 Hz, 1H), 5.94 (dd, J=5.9, 1.6 Hz, 1H), 4.77 (dt, J=10.2, 3.9 Hz, 1H), 4.66–4.53 (m, 3H), 2.17 (s, 3H); MS (ESI) m/z 424 (MH^+), 446 (M+Na). Anal. calcd for $C_{20}H_{17}N_5O_6$: C, 56.74; H, 4.05; N, 16.54. Found: C, 56.79; H, 4.06; N, 16.48.

4.1.9. 1-(5′-*O*-Benzoyl-3′-*C*-cyano-2′,3′-didehydro-2′,3′-dideoxy-L-furanosyl)uridine (18). To a solution of compound **12** (800 mg, 2.0 mmol) in dichloromethane (15 mL), DMAP (1.46 g, 12.0 mmol) and DBU (60 μL, 0.4 mmol) were added at rt. The reaction was completed after stirring for 1 h. After removal of the solvent, the residue was purified by silica gel column chromatography (dichloromethane/methanol, 50:1) to give compound **18** (0.66 g, 97% yield) as a white solid: R_f 0.54 (CH_2Cl_2/MeOH, 10:1); mp 184–186°C; $[\alpha]_D^{24}=+66.8$ (c 0.32, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 8.31 (br, 1H), 8.01–7.48 (m, 5H), 7.24 (d, J=7.8 Hz, 1H), 7.12 (d, J=4.3 Hz, 1H), 6.78 (s, 1H), 5.28 (m, 1H), 5.19 (d, J=7.8 Hz, 1H), 4.88 (dd, J=12.9, 3.1 Hz, 1H), 4.63 (dd, J=12.9, 2.7 Hz, 1H); MS (ESI) m/z 362 (M+Na). Anal. calcd for $C_{17}H_{13}N_3O_5$: C, 60.18; H, 3.86; N, 12.38. Found: C, 60.20; H, 3.93; N, 12.27.

4.1.10. 1-(5′-*O*-Benzoyl-3′-*C*-cyano-2′,3′-didehydro-3′-deoxy-L-furanosyl)thymidine (19). Using the same procedure as described for **18**, compound **13** (1.00 g, 2.4 mmol) was reacted with DMAP (1.46 g, 12.0 mmol) and DBU (60 μL, 0.4 mmol) in dichloromethane (15 mL) to give compound **19** (820 mg, 96% yield) as a white solid: R_f 0.59 (CH_2Cl_2/MeOH, 10:1); mp 206–207°C; $[\alpha]_D^{25}=+69.3$ (c 0.55, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 8.28 (br, 1H), 8.02–7.46 (m, 5H), 7.11 (dd, J=4.4, 1.2 Hz, 1H), 6.96 (s, 1H), 6.81 (s, 1H), 5.28 (m, 1H), 4.87 (dd, J=12.9, 2.8 Hz, 1H), 4.58 (dd, J=12.9, 3.1 Hz, 1H), 1.37 (s, 3H); MS (ESI) m/z 354 (MH^+), 376 (M+Na). Anal. calcd for $C_{18}H_{15}N_3O_5 \cdot 0.4H_2O$: C, 59.96; H, 4.42; N, 11.65. Found: C, 59.97; H, 4.23; N, 11.54.

4.1.11. 1-(5′-*O*-Benzoyl-3′-*C*-cyano-2′,3′-didehydro-2′,3′-dideoxy-L-furanosyl)-*N*^{4}-benzoylcytidine (20). Using the same procedure as described for **18**, compound **14** (1.2 g, 2.4 mmol) was reacted with DMAP (1.46 g, 12.0 mmol) and DBU (60 μL, 0.4 mmol) in dichloromethane (15 mL) to give compound **20** (1.0 g, 95% yield) as a white solid: R_f 0.38 (hexanes/ethyl acetate, 1:2); mp 181–183°C; $[\alpha]_D^{27}=-61.5$ (c 0.27, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.68 (br, 1H), 7.95–7.43 (m, 12H), 7.05 (m, 2H), 5.39 (m, 1H), 4.79 (dd, J=12.9, 2.8 Hz, 1H), 4.71 (dd, J=12.9, 3.1 Hz, 1H); MS (ESI) m/z 443 (MH^+). Anal. calcd for $C_{24}H_{18}N_4O_5$: C, 65.15; H, 4.10; N, 12.66. Found: C, 65.17; H, 4.09; N, 12.55.

4.1.12. 1-(5′-*O*-Benzoyl-3′-*C*-cyano-2′,3′-didehydro-2′,3′-dideoxy-L-furanosyl)cytidine (21). To a solution of compound **20** (900 mg, 2.0 mmol) in AcOH–Py (10 mL, 1:4 v/v), 85% hydrazine hydrate (0.7 mL, 12.0 mmol) was added at rt. After continually stirring for 24 h, acetone (5 mL) was added, and stirred for 30 min more. After removal of the solvent, the residue was purified by silica gel column chromatography (dichloromethane/methanol, 50:1–30:1) to give compound **21** (616 mg, 91% yield) as a white solid: R_f 0.27 (CH_2Cl_2/MeOH, 10:1); mp 184–187°C; $[\alpha]_D^{24}=+62.2$ (c 0.29, MeOH); ^1H NMR (CD_3OD) δ 8.01–7.49 (m, 5H), 7.44 (d, J=7.5 Hz, 1H), 7.06 (m, 2H), 5.46 (d, J=7.5 Hz, 1H), 5.34 (m, 1H), 4.75 (dd, J=12.7, 3.3 Hz, 1H), 4.62 (dd, J=12.7, 3.3 Hz, 1H); MS (ESI) m/z

339 (MH^+). Anal. calcd for $C_{17}H_{14}N_4O_4$: C, 60.35; H, 4.17; N, 16.56. Found: C, 60.58; H, 3.96; N, 16.58.

4.1.13. 1-(5′-*O*-Benzoyl-3′-*C*-cyano-3′-deoxy-L-ribofuranosyl)uracil (22). Using the same procedure as described for **21**, compound **12** (1.00 g, 2.5 mmol) was selectively deprotected by 85% hydrazine hydrate (0.9 mL, 15 mmol) in AcOH–Py (10 mL, 1:4 v/v) to give compound **22** (805 mg, 90% yield), as a white foam: R_f 0.43 (CH_2Cl_2/MeOH, 10:1); $[\alpha]_D^{25}=-16.4$ (*c* 0.35, MeOH); ^1H NMR ($CDCl_3$) δ 8.03–7.46 (m, 6H), 5.71 (s, 1H), 5.51 (d, *J*=7.0 Hz, 1H), 4.89–4.66 (m, 4H), 3.36 (dd, *J*=10.5, 5.4 Hz, 1H); MS (ESI) *m/z* 358 (MH^+). Anal. calcd for $C_{17}H_{15}N_3O_6$: C, 57.14; H, 4.23; N, 11.76. Found: C, 57.34; H, 4.54; N, 11.75.

4.1.14. 1-(5′-*O*-Benzoyl-3′-*C*-cyano-3′-deoxy-L-ribofuranosyl)thymine (23). Using the same procedure as described for **21**, compound **13** (1.00 g, 2.4 mmol) was selectively deprotected by 85% hydrazine hydrate (0.9 mL, 15 mmol) in AcOH–Py (10 mL, 1:4 v/v) to give compound **23** (817 mg, 91% yield) as a white solid: R_f 0.44 (CH_2Cl_2/MeOH, 10:1); mp 124–126°C, $[\alpha]_D^{23}=+12.4$ (*c* 0.52, MeOH); ^1H NMR (CD_3OD) δ 8.10–7.38 (m, 5H), 7.37 (s, 1H), 5.69 (d, *J*=1.6 Hz, 1H), 4.77 (dd, *J*=12.2, 3.5 Hz, 1H), 4.73–4.67 (m, 2H), 4.59 (dd, *J*=12.2, 3.8 Hz, 1H), 3.76 (dd, *J*=10.1, 5.7 Hz, 1H), 1.65 (s, 3H); MS (ESI) *m/z* 372 (MH^+). Anal. calcd for $C_{18}H_{17}N_3O_6$: C, 58.22; H, 4.61; N, 11.32. Found: C, 58.34; H, 4.88; N, 10.97.

4.1.15. 1-(5′-*O*-Benzoyl-3′-*C*-cyano-3′-deoxy-L-ribofuranosyl)cytosine (24). Using the same procedure as described for **21**, compound **14** (1.00 g, 2.0 mmol) was selectively deprotected by 85% hydrazine hydrate (0.7 mL, 12.0 mmol) in AcOH–Py (10 mL, 1:4 v/v) to give compound **24** (631 mg, 89% yield) as a white solid: R_f 0.1 (CH_2Cl_2/MeOH, 10:1); mp 234–236°C (dec.); $[\alpha]_D^{24}=-58.2$ (*c* 0.11, MeOH); ^1H NMR (CD_3OD) δ 8.10–7.50 (m, 6H), 5.70 (d, *J*=7.3 Hz, 1H), 5.69 (s, 1H), 4.75–4.63 (m, 4H), 3.61 (dd, *J*=10.1, 5.1 Hz, 1H); MS (ESI) *m/z* 357 (MH^+). Anal. calcd for $C_{17}H_{16}N_4O_5$: C, 57.30; H, 4.53; N, 15.72. Found: C, 57.09; H, 4.61; N, 15.83.

4.1.16. N^6-Benzoyl-9-(5′-*O*-benzoyl-3′-*C*-cyano-2′,3′-didehydro-2′,3′-dideoxy-L-furanosyl)adenosine (25). Using the same procedure as described for **18**, compound **15** (1.2 g, 2.3 mmol) was reacted with DMAP (1.46 g, 12.0 mmol) and DBU (60 μL, 0.4 mmol) in dichloromethane (15 mL) to give compound **25** (1.0 g, 94% yield) as a white foam: R_f 0.67 (CH_2Cl_2/MeOH, 10:1); $[\alpha]_D^{22}=+13.6$ (*c* 1, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 9.07 (br, 1H), 8.74 (s, 1H), 8.05 (s, 1H), 7.99–7.37 (m, 10H), 7.20 (d, *J*=3.1 Hz, 1H), 7.17 (s, 1H), 5.41 (m, 1H), 4.75 (dd, *J*=12.4, 4.0 Hz, 1H), 4.66 (dd, *J*=12.4, 4.2 Hz, 1H); MS (ESI) *m/z* 467 (MH^+). Anal. calcd for $C_{25}H_{18}N_6O_4$: C, 64.37; H, 3.89; N, 18.02. Found: C, 64.18; H, 4.01; N, 17.98.

4.1.17. N^2-Acetyl-6-*O*-diphenylcarbamoyl-9-(5′-*O*-benzoyl-3′-*C*-cyano-2′,3′-didehydro-2′,3′-dideoxy-L-furanosyl)guanosine (26). Using the same procedure as described for **18**, compound **16** (2.4 g, 3.6 mmol) was reacted with DMAP (1.46 g, 12.0 mmol) and DBU (60 μL, 0.4 mmol) in dichloromethane (15 mL) to give compound **26** (2.0 g, 93% yield) as a white solid: R_f 0.38 (hexanes/ethyl acetate, 1:2); mp 206–208°C; $[\alpha]_D^{24}=+11.8$ (*c* 0.55, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 8.09 (br, 1H), 7.93 (s, 1H), 7.89–7.24 (m, 15H), 7.06 (m, 1H), 7.01 (s, 1H), 5.35 (m, 1H), 4.75 (dd, *J*=12.4, 4.3 Hz, 1H), 4.62 (dd, *J*=12.4, 4.1 Hz, 1H), 2.45 (s, 3H); MS (ESI) *m/z* 616 (MH^+), 638 (M+Na). Anal. calcd for $C_{33}H_{25}N_7O_6$: C, 64.39; H, 4.09; N, 15.93. Found: C, 64.42; H, 4.14; N, 15.83.

4.1.18. 9-(5′-*O*-Benzoyl-3′-*C*-cyano-2′,3′-didehydro-2′,3′-dideoxy-L-furanosyl)inosine (27). Using the same procedure as described for **18**, compound **17** (1.10 g, 2.6 mmol) was reacted with DMAP (1.46 g, 12.0 mmol) and DBU (60 μL, 0.4 mmol) in dichloromethane (15 mL) to give compound **27** (897 mg, 95% yield) as a white solid: R_f 0.40 (CH_2Cl_2/MeOH, 10:1); mp 214–216°C; $[\alpha]_D^{22}=+31.6$ (*c* 0.36, MeOH); ^1H NMR (CD_3OD) δ 7.81–7.28 (m, 7H), 6.98 (m, 2H), 5.26 (m, 1H), 4.59–4.51 (m, 2H); MS (ESI) *m/z* 364 (MH^+). Anal. calcd for $C_{18}H_{13}N_5O_4{\cdot}0.4H_2O$: C, 58.35; H, 3.75; N, 18.90. Found: C, 58.53; H, 3.66; N, 18.68.

4.1.19. 9-(5′-*O*-Benzoyl-3′-*C*-cyano-2′,3′-didehydro-2′,3′-dideoxy-L-furanosyl)adenosine (28). Using the same procedure as described for **21**, compound **25** (900 mg, 1.9 mmol) was selectively deprotected by 85% hydrazine hydrate (0.7 mL, 12.0 mmol) in AcOH–Py (10 mL, 1:4 v/v) to give compound **28** (615 mg, 88% yield) as a white solid: R_f 0.35 (CH_2Cl_2/MeOH, 10:1); mp 236–238°C (dec.); $[\alpha]_D^{26}=+69.27$ (*c* 0.19, MeOH); ^1H NMR (CD_3OD) δ 8.19 (s, 1H), 8.02 (s, 1H), 7.91–7.43 (m, 5H), 7.34 (m, H), 7.19 (m, 1H), 5.47 (m, 1H), 4.73 (dd, *J*=12.4, 4.0 Hz, 1H), 4.65 (dd, *J*=12.4, 4.0 Hz, 1H), MS (ESI) *m/z* 363 (MH^+). Anal. calcd for $C_{18}H_{14}N_6O_3$: C, 59.67; H, 3.89; N, 23.19. Found: C, 59.48; H, 4.01; N, 22.98.

4.1.20. N^2-Acetyl-9-(5′-*O*-benzoyl-3′-*C*-cyano-2′,3′-didehydro-2′,3′-dideoxy-L-furanosyl)guanosine (29). Using the same procedure as described for **21**, compound **26** (1.85 g, 3 mmol) was selectively deprotected by 85% hydrazine hydrate (1 mL, 17 mmol) in AcOH–Py (10 mL, 1:4 v/v) to give compound **29** (1.07 g, 85% yield) as a white foam: R_f 0.5 (CH_2Cl_2/MeOH, 10:1); $[\alpha]_D^{22}=+70.0$ (*c* 0.28, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 12.00 (br, 1H), 9.95 (br, 1H), 8.01–7.45 (m, 6H), 6.90–6.88 (m, 2H), 5.55 (dd, *J*=11.6, 7.6 Hz, 1H), 5.36 (m, 1H), 4.40 (dd, *J*=11.6, 4.8 Hz, 1H), 2.36 (s, 3H); MS (ESI) *m/z* 421 (MH^+). Anal. calcd for $C_{20}H_{16}N_6O_5$: C, 57.14; H, 3.84; N, 19.99. Found: C, 57.02; H, 3.92; N, 20.03.

4.1.21. 9-(5′-*O*-Benzoyl-3′-*C*-cyano-3′-deoxy-L-ribofuranosyl)adenine (30). Using the same procedure as described for **21**, compound **15** (1.00 g, 1.9 mmol) was selectively deprotected by 85% hydrazine hydrate (0.7 mL, 12.0 mmol) in AcOH–Py (10 mL, 1:4 v/v) to give compound **30** (636 mg, 88% yield) as a white solid: R_f 0.34 (CH_2Cl_2/MeOH, 10:1); mp 125–127°C; $[\alpha]_D^{25}=+14.9$ (*c* 0.29, MeOH); ^1H NMR (CD_3OD) δ 8.18 (s, 1H), 8.03 (s, 1H), 7.90–7.40 (m, 5H), 6.06 (d, *J*=1.2 Hz, 1H), 5.14 (d, *J*=4.5 Hz, 1H), 4.79 (dt, *J*=10.2, 3.6 Hz, 1H), 4.72 (dd, *J*=12.4, 3.7 Hz, 1H), 4.62 (dd, *J*=12.4, 3.5 Hz, 1H), 4.42 (dd, *J*=10.2, 5.3 Hz, 1H); MS (ESI) *m/z* 381 (MH^+). Anal. calcd for $C_{18}H_{16}N_6O_4$: C, 56.84; H, 4.24; N, 22.10. Found: C, 57.11; H, 4.24; N, 21.97.

4.1.22. N^2-Acetyl-9-(5′-*O*-benzoyl-3′-*C*-cyano-3′-deoxy-L-ribofuranosyl)guanine (31). Using the same procedure as described for **21**, compound **16** (2 g, 3 mmol) was selectively deprotected by 85% hydrazine hydrate (1.2 mL, 20 mmol) in AcOH–Py (15 mL, 1:4 v/v) to give compound **31** (1.04 g, 80% yield) as a white solid: R_f 0.37 (CH_2Cl_2/MeOH, 10:1); mp 219–220°C; $[\alpha]_D^{24}=-52.8$ (*c* 0.61, acetone); ^{1}H NMR (CD_3OD) δ 7.99 (s, 1H), 7.85–7.35 (m, 5H), 5.96 (s, 1H), 5.03 (d, *J*=5.1 Hz, 1H), 4.77 (m, 1H), 4.74 (m, 1H), 4.47 (dd, *J*=10.2, 5.1 Hz, 1H), 2.12 (s, 3H); MS (ESI) *m*/*z* 439 (MH^+). Anal. calcd for $C_{20}H_{18}N_6O_6$: C, 54.79; H, 4.14; N, 19.17. Found: C, 54.41; H, 4.28; N, 19.38.

4.1.23. 9-(5′-*O*-Benzoyl-3′-*C*-cyano-3′-deoxy-L-ribofuranosyl)hypoxanthine (32). Using the same procedure as described for **21**, compound **17** (1.00 g, 2.4 mmol) was selectively deprotected by 85% hydrazine hydrate (0.9 mL, 15 mmol) in AcOH–Py (10 mL, 1:4 v/v) to give compound **32** (783 mg, 87% yield) as a white solid: R_f 0.2 (CH_2Cl_2/MeOH, 10:1); mp 174–176°C; $[\alpha]_D^{26}=+18.5$ (*c* 0.72, acetone); ^{1}H NMR (CD_3OD) δ 8.16 (s, 1H), 7.93–7.43 (m, 6H), 6.07 (s, 1H), 5.07 (d, *J*=5.5 Hz, 1H), 4.79–4.64 (m, 3H), 4.30 (dd, *J*=10.2, 5.1 Hz, 1H); MS (ESI) *m*/*z* 382 (MH^+). Anal. calcd for $C_{18}H_{15}N_5O_5$: C, 56.69; H, 3.96; N, 18.37. Found: C, 56.34; H, 4.07; N, 18.06.

4.1.24. 1-(3′-*C*-Cyano-2′,3′-didehydro-2′,3′-dideoxy-L-furanosyl)uridine (33). To a solution of compound **18** (550 mg, 1.6 mmol) in methanol (15 mL) was added potassium carbonate (56 mg, 0.4 mmol) at 0°C. After stirring at rt for 20 min more, the reaction was quenched with acetic acid (50 μL). After removal of the solvent, the residue was purified by silica gel column chromatography (dichloromethane/methanol, 50:1–25:1) to give compound **33** (270 mg, 71% yield) as a white solid: R_f 0.35 (CH_2Cl_2/MeOH, 10:1); mp 138–141°C; $[\alpha]_D^{22}=-60.7$ (*c* 0.18, MeOH); UV (MeOH) λ_{max} 257.5 nm (ε 11004); ^{1}H NMR (CD_3OD) δ 7.89 (d, *J*=8.1 Hz, 1H), 7.08 (m, 1H), 6.90 (t, *J*=1.8 Hz, 1H), 5.67 (d, *J*=8.1 Hz, 1H), 5.01 (m, 1H), 3.86 (s, 2H); ^{13}C NMR (CD_3OD) δ 164.9, 151.1, 141.8, 141.0, 119.2, 112.0, 101.8, 89.7, 87.2, 60.8; MS (ESI) *m*/*z* 258 (M+Na). Anal. calcd for $C_{10}H_9N_3O_4{\cdot}0.5H_2O$: C, 49.18; H, 4.13; N, 17.21. Found: C, 49.32; H, 4.08; N, 16.90.

4.1.25. 1-(3′-*C*-Cyano-2′,3′-didehydro-3′-deoxy-L-furanosyl)thymidine (34). Using the same procedure as described for **33**, compound **19** (650 mg, 1.8 mmol) was treated with potassium carbonate (60 mg, 0.43 mmol) in methanol (15 mL) to give compound **34** (312 mg, 68% yield) as a white solid: R_f 0.37 (CH_2Cl_2/MeOH, 10:1); mp 200–202°C; $[\alpha]_D^{26}=-17.1$ (*c* 0.5, MeOH) (the optical rotation for the D-isomer[7a] has not been reported); UV (MeOH) λ_{max} 263 nm (ε 13400); ^{1}H NMR (CD_3OD) δ 7.75 (s, 1H), 7.09 (dd, *J*=3.9, 1.5 Hz, 1H), 6.90 (t, *J*=1.5 Hz, 1H), 5.00 (m, 1H), 3.88 (s, 2H), 1.84 (s, 3H); ^{13}C NMR (CD_3OD) δ 166.4, 152.5, 142.6, 138.6, 120.3, 113.3, 111.8, 90.7, 88.3, 62.0, 12.4; MS (ESI) *m*/*z* 250 (MH^+). Anal. calcd for $C_{11}H_{11}N_3O_4$: C, 53.01; H, 4.45; N, 16.86. Found: C, 52.97; H, 4.51; N, 16.53.

4.1.26. 1-(3′-*C*-Cyano-2′,3′-didehydro-2′,3′-dideoxy-L-furanosyl)cytidine (35). Using the same procedure as described for **33**, compound **21** (500 mg, 1.5 mmol) was treated with potassium carbonate (50 mg, 0.36 mmol) in methanol (15 mL) to give compound **35** (232 mg, 67% yield) as a white solid: R_f 0.43 (CH_2Cl_2/MeOH, 4:1); mp 250–252°C (dec.); $[\alpha]_D^{24}=-116.4$ (*c* 0.079, MeOH); UV (MeOH) λ_{max} 267.5 nm (ε 8853); ^{1}H NMR (CD_3OD) δ 7.92 (d, *J*=7.5 Hz, 1H), 7.12 (dd, *J*=3.9, 1.6 Hz, 1H), 6.90 (t, *J*=1.8 Hz, 1H), 5.88 (d, *J*=7.5 Hz, 1H), 5.02 (m, 1H), 3.87 (m, 2H); ^{13}C NMR (CD_3OD) δ 166.6, 156.9, 142.4, 142.2, 118.4, 112.5, 95.4, 90.8, 87.1, 61.0; MS (ESI) *m*/*z* 235 (MH^+). Anal. calcd for $C_{10}H_{10}N_4O_3$: C, 51.28; H, 4.30; N, 23.92. Found: C, 51.35; H, 4.28; N, 23.79.

4.1.27. 1-(3′-*C*-Cyano-3′-deoxy-L-ribofuranosyl)uracil (36). Using the same procedure as described for **33**, compound **22** (700 mg, 2.0 mmol) was treated with potassium carbonate (70 mg, 0.5 mmol) in methanol (15 mL) to give compound **36** (411 mg, 83% yield) as a white foam: R_f 0.3 (CH_2Cl_2/MeOH, 9:1); $[\alpha]_D^{25}=-44.8$ (*c* 0.3, MeOH); UV (MeOH) λ_{max} 260 nm (ε 9279); ^{1}H NMR (CD_3OD) δ 8.01 (d, *J*=8.0 Hz, 1H), 5.75 (s, 1H), 5.64 (d, *J*=8.0 Hz, 1H), 4.56 (d, *J*=5.1 Hz, 1H), 4.44 (dt, *J*=10.2, 2.3 Hz, 1H), 4.02 (dd, *J*=12.9, 2.4 Hz, 1H), 3.76 (dd, *J*=12.9, 2.7 Hz, 1H), 3.49 (dd, *J*=10.2, 5.1 Hz, 1H); ^{13}C NMR (CD_3OD) δ 165.1, 150.8, 141.2, 115.9, 101.0, 93.4, 82.8, 75.4, 59.5, 34.6; MS (ESI) *m*/*z* 276 (M+Na). Anal. calcd for $C_{10}H_{11}N_3O_5$: C, 47.43; H, 4.38; N, 16.59. Found: C, 47.20; H, 4.27; N, 16.55.

4.1.28. 1-(3′-*C*-Cyano-3′-deoxy-L-ribofuranosyl)thymine (37). Using the same procedure as described for **33**, compound **23** (700 mg, 1.9 mmol) was treated with potassium carbonate (70 mg, 0.5 mmol) in methanol (15 mL) to give compound **37** (423 mg, 84% yield) as a white solid: R_f 0.29 (CH_2Cl_2/MeOH, 10:1); mp 108–110°C; $[\alpha]_D^{24}=-20.5$ (*c* 0.37, MeOH); UV (MeOH) λ_{max} 264.5 nm (ε 9717); ^{1}H NMR (CD_3OD) δ 7.85 (s, 1H), 5.76 (s, 1H), 4.54 (d, *J*=5.3 Hz, 1H), 4.42 (dt, *J*=10.0, 2.4 Hz, 1H), 4.02 (dd, *J*=12.8, 2.3 Hz, 1H), 3.76 (dd, *J*=12.8, 2.6 Hz, 1H), 3.52 (dd, *J*=10.0, 5.3 Hz, 1H), 1.84 (s, 3H); ^{13}C NMR (CD_3OD) δ 164.5, 151.0, 136.8, 117.7, 109.7, 92.0, 82.1, 74.8, 60.3, 35.6, 12.9; MS (ESI) *m*/*z* 268 (MH^+). Anal. calcd for $C_{11}H_{13}N_3O_5$: C, 49.44; H, 4.90; N, 15.72. Found: C, 49.25; H, 4.94; N, 15.58.

4.1.29. 1-(3′-*C*-Cyano-3′-deoxy-L-ribofuranosyl)cytosine (38). Using the same procedure as described for **33**, compound **24** (500 mg, 1.4 mmol) was treated with potassium carbonate (70 mg, 0.5 mmol) in methanol (15 mL) to give compound **38** (287 mg, 81% yield) as a white solid: R_f 0.25 (CH_2Cl_2/MeOH, 3:1); mp 126–129°C; $[\alpha]_D^{23}=-48.9$ (*c* 1.8, MeOH); UV (MeOH) λ_{max} 270.5 nm (ε 6705); ^{1}H NMR (CD_3OD) δ 8.05 (d, *J*=7.5 Hz, 1H), 5.85 (d, *J*=7.5 Hz, 1H), 5.75 (s, 1H), 4.51 (d, *J*=4.9 Hz, 1H), 4.46 (dt, *J*=10.4, 2.4 Hz, 1H), 4.04 (dd, *J*=12.8, 2.2 Hz, 1H), 3.78 (dd, *J*=12.8, 2.5 Hz, 1H), 3.42 (dd, *J*=10.4, 4.9 Hz, 1H); ^{13}C NMR (CD_3OD) δ 166.6, 156.9, 141.5, 116.0, 94.4, 94.1, 82.8, 75.8, 59.4, 34.4; MS (ESI) *m*/*z* 253 (MH^+). Anal. calcd for $C_{10}H_{12}N_4O_4$: C, 47.62; H, 4.80; N, 22.21. Found: C, 47.49; H, 4.94; N, 22.09.

4.1.30. 9-(3′-*C*-Cyano-2′,3′-didehydro-2′,3′-dideoxy-L-furanosyl)adenosine (39). Using the same procedure as described for **33**, compound **28** (500 mg, 1.4 mmol) was

treated with potassium carbonate (50 mg, 0.36 mmol) in methanol (15 mL) to give compound **39** (253 mg, 71% yield) as a white solid: R_f 0.45 (CH_2Cl_2/MeOH, 8:1); mp 223–225°C (dec.); $[\alpha]_D^{23}=-41.4$ (*c* 0.13, MeOH); UV (MeOH) λ_{max} 259 nm (ε 14703); ^{1}H NMR (CD_3OD) δ 8.30 (s, 1H), 8.20 (s, 1H), 7.18 (dd, *J*=3.5, 1.6 Hz, 1H), 7.08 (t, *J*=1.8 Hz, 1H), 5.16 (m, 1H), 3.88 (m, 2H); ^{13}C NMR (CD_3OD) δ 156.8, 153.5, 149.6, 142.4, 140.0, 119.2, 118.2, 113.8, 88.5, 87.7, 61.9; MS (ESI) *m/z* 259 (MH^+). Anal. calcd for $C_{11}H_{10}N_6O_2$: C, 51.16; H, 3.90; N, 32.54. Found: C, 51.09; H, 3.93; N, 32.35.

4.1.31. 9-(3′-*C*-Cyano-2′,3′-didehydro-2′,3′-dideoxy-L-furanosyl)guanosine (40). Using the same procedure as described for **33**, compound **29** (900 mg, 2.1 mmol) was treated with potassium carbonate (70 mg, 0.5 mmol) in methanol (15 mL) to give compound **40** (205 mg, 35% yield) as a white foam: R_f 0.45 (CH_2Cl_2/MeOH, 8:1); $[\alpha]_D^{26}=-31.8$ (*c* 0.1, MeOH); UV (MeOH) λ_{max} 251 nm (ε 15014);); ^{1}H NMR (D_2O+DMSO-d_6) δ 7.94 (s, 1H), 7.04 (s, 1H), 6.91 (s, 1H), 5.10 (m, 1H), 3.86 (m, 2H). ^{13}C NMR (D_2O+DMSO-d_6) δ 157.4, 154.7, 151.4, 142.3, 136.2, 118.2, 116.8, 113.8, 87.8, 87.6, 61.8. MS (ESI) *m/z* 275 (MH^+). Anal. calcd for $C_{11}H_9N_5O_3$: C, 48.18; H, 3.68; N, 30.65. Found: C, 48.23; H, 3.75; N, 30.56.

4.1.32. 9-(3′-*C*-Cyano-2′,3′-didehydro-2′,3′-dideoxy-L-furanosyl)inosine (41). Using the same procedure as described for **33**, compound **27** (700 mg, 1.9 mmol) was treated with potassium carbonate (60 mg, 0.43 mmol) in methanol (15 mL) to give compound **41** (325 mg, 65% yield) as a white solid: R_f 0.26 (CH_2Cl_2/MeOH, 8:1); mp 150–152°C; $[\alpha]_D^{22}=-37.4$ (*c* 0.4, MeOH); UV (MeOH) λ_{max} 244 nm (ε 12378); ^{1}H NMR (CD_3OD) δ 8.30 (s, 1H), 8.07 (s, 1H), 7.20 (dd, *J*=3.3, 1.9 Hz, 1H), 7.09 (t, *J*=1.9 Hz, 1H), 5.15 (m, 1H), 3.87 (m, 2H); ^{13}C NMR (CD_3OD) δ 157.7, 148.6, 146.0, 140.0, 139.6, 124.0, 119.1, 112.0, 88.8, 88.1, 61.0; MS (ESI) *m/z* 260 (MH^+). Anal. calcd for $C_{11}H_9N_5O_3{\cdot}0.9H_2O$: C, 47.97; H, 3.95; N, 25.43. Found: C, 48.15; H, 4.00; N, 25.14.

4.1.33. 9-(3′-*C*-Cyano-3′-deoxy-L-ribofuranosyl)adenine (42). Using the same procedure as described for **33**, compound **30** (500 mg, 1.3 mmol) was treated with potassium carbonate (70 mg, 0.5 mmol) in methanol (15 mL) to give compound **42** (276 mg, 76% yield) as a white solid: R_f 0.14 (CH_2Cl_2/MeOH, 10:1); mp 236–238°C (dec.); $[\alpha]_D^{23}=+45.3$ (*c* 0.11, MeOH); UV (MeOH) λ_{max} 258.5 nm (ε 14894); ^{1}H NMR (D_2O+DMSO-d_6) δ 8.34 (s, 1H), 8.15 (s, 1H), 5.99 (d, *J*=2.0 Hz, 1H), 4.84 (dd, *J*=5.6, 2.0 Hz, 1H), 4.40 (m, 1H), 3.90 (dd, *J*=9.1, 5.6 Hz, 1H), 3.76–3.51 (m, 2H); ^{13}C NMR (D_2O+DMSO-d_6) δ 156.8, 153.3, 149.4, 139.9, 119.7, 117.9, 91.2, 82.6, 74.9, 61.1, 36.4; MS (ESI) *m/z* 277 (MH^+). Anal. calcd for $C_{11}H_{12}N_6O_3$: C, 47.83; H, 4.38; N, 30.42. Found: C, 47.47; H, 4.46; N, 30.27.

4.1.34. 9-(3′-*C*-Cyano-3′-deoxy-L-ribofuranosyl)guanine (43). Using the same procedure as described for **33**, compound **31** (800 mg, 1.9 mmol) was treated with potassium carbonate (70 mg, 0.5 mmol) in methanol (15 mL) to give compound **43** (350 mg, 63% yield) as a white solid: mp 235–237°C (dec.); $[\alpha]_D^{25}=+22.0$ (*c* 0.08, MeOH–H_2O (1:1)); UV (MeOH) λ_{max} 251.5 nm (ε 15513); ^{1}H NMR (D_2O+DMSO-d_6) δ 7.88 (s, 1H), 5.77 (s, 1H), 4.71 (d, *J*=5.7 Hz, 1H), 4.31 (m, 1H), 3.93–3.67 (m, 2H), 3.60 (m, 1H); ^{13}C NMR (D_2O+DMSO-d_6) δ 157.4, 154.4, 151.4, 136.3, 118.0, 117.4, 90.7, 82.4, 75.1, 61.4, 36.9; MS (ESI) *m/z* 293 (MH^+). Anal. calcd for $C_{11}H_{12}N_6O_4$: C, 45.21; H, 4.14; N, 28.76. Found: C, 45.17; H, 4.26; N, 28.48.

4.1.35. 9-(3′-*C*-Cyano-3′-deoxy-L-ribofuranosyl)hypoxanthine (44). Using the same procedure as described for **33**, compound **32** (650 mg, 1.7 mmol) was treated with potassium carbonate (70 mg, 0.5 mmol) in methanol (15 mL) to give compound **44** (368 mg, 78% yield) as a white solid: mp 148–150°C; $[\alpha]_D^{23}=+42.1$ (*c* 0.6, MeOH); UV (MeOH) λ_{max} 245.5 nm (ε 11590); ^{1}H NMR (CD_3OD) δ 8.36 (s, 1H), 8.07 (s, 1H), 6.10 (d, *J*=1.5 Hz, 1H), 4.91 (dd, *J*=5.4, 1.9 Hz, 1H), 4.55 (dt, *J*=9.8, 2.7 Hz, 1H), 4.01 (dd, *J*=12.7, 2.9 Hz, 1H), 3.93 (dd, *J*=9.8, 5.4 Hz, 1H), 3.79 (dd, *J*=12.7, 2.9 Hz, 1H); ^{13}C NMR (CD_3OD) δ 157.6, 148.1, 145.7, 139.4, 124.7, 116.1, 92.2, 83.0, 75.6, 60.1, 35.3; MS (ESI) *m/z* 278 (MH^+). Anal. calcd for $C_{11}H_{11}N_5O_4{\cdot}0.5H_2O$: C, 46.16; H, 4.23; N, 24.47. Found: C, 46.20; H, 4.19; N, 24.40.

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