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Note

Novel ring transformation of 5-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-isoxazole-4-carbaldehyde with 1,2-diaminobenzenes to 3-cyano-1,5-benzodiazepine *C*-nucleosides

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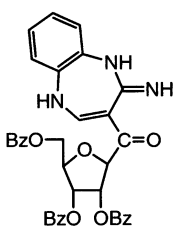
Abstract

Syntheses of 3-cyano-7- and 8-substituted-4-(β-D-ribofuranosyl)-1*H*-1,5-benzodiazepines were reported. Treatment of isoxazole carbaldehyde with 1,2-diamino-4-nitrobenzene in chloroform gave a Schiff's base, 4-(2-amino-5-nitrophenyl)iminomethyl-5-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)isoxazole in 82% yield with no trace of the other regioisomer. The cyclocondensation of the resulting Schiff's base in benzene containing trifluoroacetic acid (TFA) gave 3-cyano-8-nitro-4-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1*H*-1,5-benzodiazepine in 49% yield. The same reaction of isoxazole carbaldeyde with 1,2-diamino-4-methoxy- and 4-chlorobenzenes afforded the corresponding Schiff's bases. Extending the reaction time for Schiff's base gave the corresponding cyanobenzodiazepines in good yields. Debenzoylation of the compounds with sodium methoxide produced deprotected *C*-nucleosides.

Keywords: Synthesis; *C*-Nucleoside; Cyclocondensation; Isoxazole carbaldehyde; 3-Cyano-1,5-benzodiazepine; 1,5-Benzodiazepine *C*-nucleoside

In a recent report from our laboratory, we described the reaction of *o*-phenylenediamine with 5-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-isoxazole-4-carbaldehyde (**1**) in chloroform at room temperature to give 2-imino-3-[1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)oxo]-1*H*-,5*H*-1,5-benzodiazepine (a) homo-*C*-nucleoside [1]. In connection with our continuing interests in *C*-nucleoside chemistry, we wish to report the synthesis of benzodiazepine *C*-nucleosides, having a carbon–carbon ribosylic linkage, by ring transformation of the isozaxole carbaldehyde (**1**), which can be obtained from an enaminone glycoside by our previously published procedure [2] (Scheme 1).



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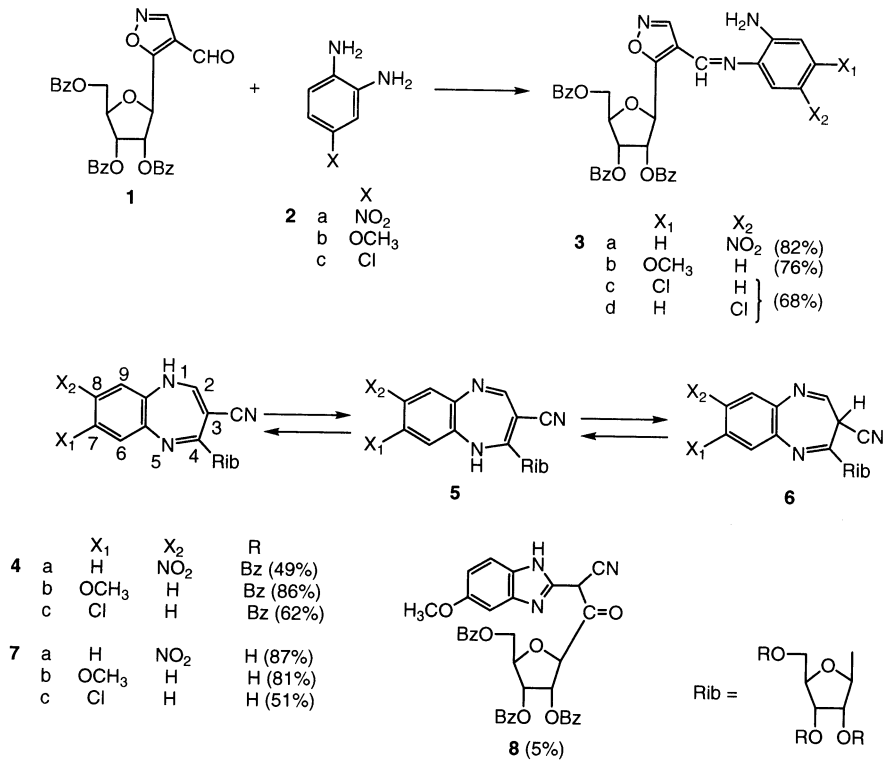
Treatment of isoxazole carbaldehyde (**1**) with 1,2-diamino-4-nitrobenzene (**2a**) in chloroform at room temperature for 5 days gave Schiff's base **3a** in 82% yield with no trace of the other regioisomer. High reaction temperature gave lower yields. We assume that the condensation reaction will take place between the aldehyde group of **1** and the more nucleophilic 2-amino group of **2a**, as this route is favored over reaction with 1-amino group due to the electron-withdrawing effect of the nitro group. The cyclocondensation of the Schiff's base **3a** in benzene containing trifluoroacetic acid (TFA) at room temperature for 2 h gave 3-cyano-8-nitro-4-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1*H*-1,5-benzodiazepine (**4a**) in 49% yield.

3-Cyanobenzodiazepine **4a** was characterized by FABMS and ^{1}H and ^{13}C NMR spectra. The NMR information indicates that the product in dimethyl sulfoxide is actually in the form of isomers **4** and **5** in a ratio of about 1:1 and not in other tautomeric forms such as **6**. Two single sharp peaks for the diazepine ring hydrogens were observed at δ 9.23 and 9.26, respectively. A broad N–H absorption is indistinctly split into two peaks. Formation of **4a** from Schiff's base **3a** most probably proceeded by the protonation of the oxygen in the isoxazole ring to give the ring-opened intermediate, which was further cyclized to **4a**. Removal of protecting groups in compound **4a** with sodium methoxide was readily accomplished and afforded 3-cyano-8-nitro-4-(β-D-ribofuranosyl)-1*H*-1,5-benzodiazepine (**7a**) in 87% yield.

Next, the reaction between 1,2-diamino-4-methoxybenzene (**2b**) and **1** afforded two compounds 4-(2-amino-4-methoxyphenyl)iminomethyl-5-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)isoxazole (**3b**) and 3-cyano-7-methoxy-4-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1*H*-1,5-benzodiazepine (**4b**) in 76 and 14% yield, respectively. Complete disappearance of starting material **1** was observed after 22 h. Extending the reaction time for 16 days increased the yield of the desired compound **4b** (86%), and small amounts of 2-cyano-2-(5-methoxybenzimidazolyl)-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)ethane-1-one (**8**) (5%), which resulted from ring contraction of **4b**. In NOE studies carried out on **8**, the signal corresponding to the methine proton of position 2 was not observed. The missing signal may



Scheme 1.

be attributed to rapid exchange occuring between tautomeric forms [3]. The ring contraction of 1,5-benzodiazepine into benzimidazole under basic conditions has been reported by Okamoto and Ueda [4]. A plausible explanation for the formation of **4b** involves nucleophilic attack at the hydrogen of the isoxazole C-3 by the amino group of methoxybenzene with subsequent cyclization to cyanobenzodiazepine **4b**.

When the same reaction of **1** with 1,2-diamino-4-chlorobenzene (**2c**) at room temperature for 5 h was performed, an inseparable mixture of 4-(2-amino-4- and 5-chlorophenyl)iminomethyl-5-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)isoxazole (**3c** and **3d**) in a ratio of about 4:1 was obtained in 68% yield. Extending the reaction time for 2 days gave 7-chloro-3-cyano-4-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1*H*-1,5-benzodiazepine (**4c**) in 62% yield with no trace of the other regioisomer from **3d**. The position of the substituent in compound **4c** was determined by an NOE experiment with the corresponding deprotected derivative **7c**, prepared by deprotection of **3b** with sodium methoxide. Irradiation of the OH signal (δ 5.20) in compound **7c** gave a 2.3% enhancement of the signal at δ 7.69 assignable to H-6. The data indicated that the chloro group was located at the 7-position. The stereochemistry of the C-1′ position in compounds **7a**–**c** was confirmed as β by NOE experiments (Fig. 1). Thus the NOE indicates that the β-ribofuranoside configuration has been preserved during the reaction sequence.

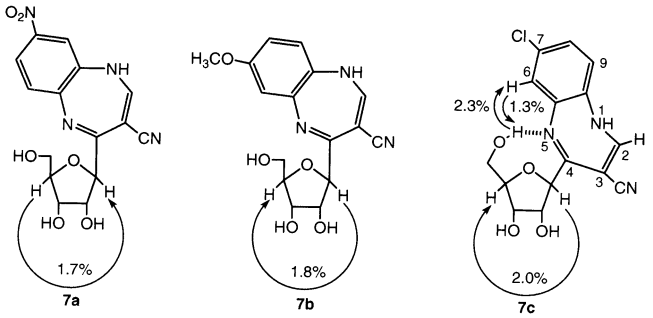


Fig. 1. NOE experiments for compounds **7a**–**c**.

1. Experimental

General.—Fast-atom bombardment mass spectra (FABMS) were run on a JMS-HX 110 spectrometer. The ^{1}H and ^{13}C NMR spectra were measured with a JNM-A-400 or an A-600 (Jeol) spectrometer, with Me_4Si as an internal standard. The IR spectrum was measured with a FT/IR-230 (Jasco) spectrometer. Optical rotations were measured with a Jasco DIP-370 polarimeter (10-cm cell) at 25 °C. Elemental analyses were carried out by the microanalysis service of the University of Meijo. Analytical thin-layer chromatography (TLC) was performed on glass plates coated with a 0.25-mm layer of Silica Gel GF254 (E. Merck). The compounds were detected by UV light (254 nm).

4-(2-Amino-5-nitrophenyl)iminomethyl-5-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-isoxazole (**3a**).—To a solution of **1** (158.9 mg, 0.294 mmol) in $CHCl_3$ (32 mL) was added 4-nitro-1,2-phenylenediamine (**2a**) (67.5 mg, 0.441 mmol). The mixture was stirred at rt for 5 days. Water was added, and the mixture was then extracted with $CHCl_3$ (3×10 mL). The extracts were combined, washed with water and dried over $MgSO_4$, and evaporated to dryness. The residual syrup was purified by PTLC with $CHCl_3$ as eluent to give 162.4 mg (82%) of **3a** as a yellow oil; ^{1}H NMR ($CDCl_3$): δ 4.67 (dd, 1 H, $J_{4',5'a}$ 4.9, $J_{5'a,5'b}$ 13.0 Hz, H-5′a), 4.85 (m, 2 H, H-4′, 5′b), 5.00 (s, 2 H, NH_2, exchanged with D_2O), 5.84 (d, 1 H, $J_{1',2'}$ 5.3 Hz, H-1′), 5.91 (dd, 1 H, $J_{2',3'} = J_{3',4'}$ 5.3 Hz, H-3′), 5.98 (dd, 1 H, $J_{1',2'} = J_{2',3'}$ 5.3 Hz, H-2′), 6.63 (d, 1 H, $J_{3,4}$ 8.8 Hz, nitrobenzene H-3), 7.36–7.57 (m, 9 H, Ph), 7.93–8.04 (m, 8 H, Ph), 8.72, 8.73 (each s, each 1 H, isoxazole H-3, –CH=N–); ^{13}C NMR ($CDCl_3$): δ 63.5 (C-5′), 72.1, 74.9, 75.9, 80.6 (C-1′, 2′, 3′, 4′), 113.1, 113.2 (Ph), 117.5 (C-4), 124.7–138.5 (Ph), 148.4 (C-3), 148.5 (Ph), 149.1 (–CH=N–), 165.2, 165.3, 166.0 (C=O), 167.7 (C-5). FABMS (nitrobenzyl alcohol as matrix): Calcd for $C_{36}H_{29}N_4O_{10}$; 677.1884 [MH]. Found: m/z 677.1926 $[MH]^+$.

3-Cyano-8-nitro-4-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-1H-1,5-benzodiazepine (**4a**).—A solution of **3a** (27.8 mg, 0.041 mmol) in benzene (2 mL) containing one drop of trifluoroacetic acid was stirred at rt for 2 h. Water was added, and then the mixture was ex-

tracted with $CHCl_3$ (3 × 10 mL). The extracts were combined, washed with water and dried over $MgSO_4$. The extracts, on evaporation, afforded a yellow oil, which was purified by PTLC with 99.5:0.5 $CHCl_3$–MeOH as eluent after four elutions.

Compound **4a**: orange oil; yield 13.1 mg (49%); R_f 0.27; IR (KBr) 2208 (CN) cm^{-1}; ^1H NMR [$(CD_3)_2SO$]: δ 4.63–4.73 (m, 2 H, H-5′), 4.92 (m, 1 H, H-4′), 6.02–6.12 (m, 2 H, H-2′, 3′), 6.41 (d, 1 H, $J_{1',2'}$ 5.1 Hz, H-1′), 7.33–7.69 (m, 9.5 H, H-6, Ph), 7.74 (d, 0.5 H, $J_{6,7}$ 8.8 Hz, H-6), 7.80–8.09 (m, 6 H, Ph), 8.14 (m, 1 H, H-7), 8.30 (m, 1 H, H-9), 9.23, 9.26 (each s, each 0.5 H, H-2), 13.38 (br, 1 H, NH, exchanged with D_2O); ^{13}C NMR ($CDCl_3$): δ 63.3 (C-5′), 71.5 (C-3′), 74.3 (C-2′), 76.4 (C-1′), 81.5 (C-4′), 110.2 (CN), 108.5, 115.9 (C-9), 111.3, 119.3 (C-6), 118.4, 119.1 (C-7), 128.3–147.9 (C-3, 5a, 8, 9a, Ph), 150.5 (C-2), 164.4, 164.6 (C-4), 165.3, 165.6, 166.5 (C=O). FABMS (nitrobenzyl alcohol as matrix): Calcd for $C_{36}H_{27}N_4O_9$; 659.1778 [MH]. Found: m/z 659.1746 $[MH]^+$.

*4-(2-Amino-4-methoxyphenyl)iminomethyl-5-(2,3,5-tri-*O*-benzoyl-β-*D*-ribofuranosyl)-isoxazole* (**3b**), *7-methoxy-3-cyano-4-(2,3,5-tri-*O*-benzoyl-β-*D*-ribofuranosyl)-1*H*-1,5-benzodiazepine* (**4b**) *and 2-cyano-2-(5-methoxybenzimidazolyl)-1-(2,3,5-tri-*O*-benzoyl-β-*D*-ribofuranosyl)ethane-1-one* (**8**).—To a solution of **1** (55.5 mg, 0.103 mmol) in $CHCl_3$ (8 mL) was added 4-methoxy-1,2-phenylenediamine (**2b**) (21.2 mg, 0.154 mmol). The mixture was stirred at rt for 16 days, and then the reaction mixture was evaporated. TLC (99:1 $CHCl_3$–MeOH) showed that the yellow syrup contained three major components (R_f 0.25, 0.16 and 0.13). The residue was purified by PTLC with 99.25:0.75 $CHCl_3$–MeOH as eluent after three elutions.

Compound **3b**: yellow oil; yield 2.5 mg (4%); R_f 0.25; ^1H NMR ($CDCl_3$): δ 3.75 (s, 3 H, OCH_3), 4.67 (br, 2 H, NH_2, exchanged with D_2O), 4.67 (dd, 1 H, $J_{4',5'a}$ 3.8, $J_{5'a,5'b}$ 11.5 Hz, H-5′a), 4.83 (m, 2 H, H-4′, 5′b), 5.82 (d, 1 H, $J_{1',2'}$ 5.1 Hz, H-1′), 5.95 (m, 2 H, H-2′, 3′), 6.19 (dd, 1 H, $J_{3,5}$ 2.6, $J_{5,6}$ 8.8 Hz, methoxybenzene H-5), 6.25 (d, 1 H, $J_{3,5}$ 2.6 Hz, methoxybenzene H-3), 6.95 (d, 1 H, $J_{5,6}$ 8.8 Hz, methoxybenzene H-6), 7.36–8.06 (m, 15 H, Ph), 8.55 (s, 1 H, isoxazole H-3), 8.70 (s, 1 H, –CH=N–); ^{13}C NMR ($CDCl_3$): δ 55.2 (OCH_3), 63.8 (C-5′), 72.3, 74.8, 75.7, 80.7 (C-1′, 2′, 3′, 4′), 100.4, 104.1, 117.3 (Ph), 118.4 (C-4), 128.4–133.7 (Ph), 142.4 (C-3), 144.0 (Ph), 149.3 (–CH=N–), 160.3 (Ph), 165.1, 165.2, 165.6, 166.2 (C-5, C=O), 167.7 (C-5). FABMS (nitrobenzyl alcohol as matrix): Calcd for $C_{37}H_{32}N_3O_9$; 662.2139 [MH]. Found: m/z 662.2132 $[MH]^+$.

Compound **4b**: pale yellow form; yield 56.4 mg (86%); R_f 0.16; IR (KBr) 2197 (CN) cm^{-1}; ^1H NMR [$(CD_3)_2SO$]: δ 3.71, 3.79 (each s, each 1.5 H, OCH_3), 4.62–4.76 (m, 2 H, H-5′), 4.89 (m, 1 H, H-4′), 6.02 (m, 1 H, H-3′), 6.10 (m, 1 H, H-2′), 6.42, 6.46 (each d, each 0.5 H, $J_{1',2'}$ 5.1 Hz, H-1′), 6.81, 6.85 (each d, each 0.5 H, $J_{8,9}$ 8.8 Hz, H-9), 7.01 (s, 1 H, H-6), 7.34–8.30 (m, 16 H, H-8, Ph), 9.17, 9.18 (each s, each 0.5 H, H-2), 12.81, 12.85 (each br, each 0.5 H, NH, exchanged with D_2O); ^{13}C NMR [$(CD_3)_2SO$]: δ 55.3, 55.5 (OCH_3), 63.5 (C-5′), 72.2 (C-3′), 74.0, 74.0 (C-2′), 74.2, 74.4 (C-1′), 79.4, 79.4 (C-4′), 94.4, 100.9 (C-6), 110.8, 111.0 (CN), 111.6, 112.9 (C-9), 111.7, 119.3 (C-8), 128.3–133.8, 138.0 (C-5a, Ph), 134.7, 144.4 (C-9a), 141.2, 142.3 (C-3), 149.6, 149.7 (C-2), 155.6, 156.3 (C-7), 165.0 (C-4), 164.5, 164.5, 164.8, 165.5 (C=O). Anal. Calcd for $C_{37}H_{29}N_3O_8 \cdot 1.4\ H_2O$; C, 66.44; H, 4.79; N, 6.28. Found: C, 66.16; H, 4.49; N, 6.11.

Compound **8**: yield 3.1 mg (5%); R_f 0.13; IR (KBr) 2195 (CN) cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.72, 3.83 (each s, each 1.5 H, OCH_3), 4.68 (dd, 1 H, $J_{4',5'a}$ 4.9, $J_{5'a,5'b}$ 11.6 Hz, H-5′a), 4.79 (m, 1 H, H-4′), 4.83 (dd, 1 H, $J_{4',5'b}$ 4.0, $J_{5'a,5'b}$ 11.6 Hz, H-5′b), 5.34 (d, 1 H, $J_{1',2'}$ 3.7 Hz, H-1′), 5.91 (dd, 1 H, $J_{2',3'}$ 5.2, $J_{3',4'}$ 6.4 Hz, H-3′), 6.04 (dd, 1 H, $J_{1',2'}$ 3.7, $J_{2',3'}$ 5.2 Hz, H-2′), 6.84–8.05 (m, 18 H, Ph), 12.60 (br, 1 H, NH, exchanged with D_2O); ^{13}C NMR ($CDCl_3$): δ 55.8 (OCH_3), 64.4 (C-5′), 65.9 (C-2), 73.1, 74.6, 79.9, 83.2 (C-1′, 2′, 3′, 4′), 96.2, 112.3, 123.8 (Ph), 119.4 (CN), 128.3–133.3 (Ph), 152.0 (benzimidazole C-2), 157.4 (Ph), 165.3, 166.2 (C=O), 187.4 (C-1). FABMS (nitrobenzyl alcohol as matrix): Calcd for $C_{37}H_{30}N_3O_9$; 660.1982 [MH]. Found: m/z 660.1990 $[MH]^+$.

*4-(2-Amino-4-chlorophenyl)iminomethyl-5-(2,3,5-tri-*O*-benzoyl-β-*D*-ribofuranosyl)-isoxazole* (**3c**) *and 4-(2-amino-5-chloro-*

*phenyl)iminomethyl-5-(2,3,5-tri-*O*-benzoyl-β-*D*-ribofuranosyl)isoxazole* (**3d**).—To a solution of **1** (87.7 mg, 0.162 mmol) in $CHCl_3$ (9 mL) was added 4-chloro-1,2-phenylenediamine (**2c**) (36.1 mg, 0.243 mmol). The mixture was stirred at rt for 5 h, and then the reaction mixture was evaporated. The residue was purified by PTLC with 99:1 $CHCl_3$–MeOH as eluent to give 73.3 mg (68%) of **3c** and **3d** as a yellow form; ^{1}H NMR ($CDCl_3$): δ 4.20 (br, 2 H, NH_2, exchanged with D_2O), 4.63–4.87 (m, 3 H, H-4′, 5′), 5.79–5.99 (m, 3 H, H-1′, 2′, 3′), 6.57 (dd, 0.8 H, $J_{3,5}$ 2.0, $J_{5,6}$ 8.5 Hz, chlorobenzene H-5), 6.60 (d, 0.2 H, $J_{3,4}$ 8.1 Hz, chlorobenzene H-3), 6.67 (d, 0.8 H, $J_{3,5}$ 2.0 Hz, chlorobenzene H-3), 6.83 (d, 0.8 H, $J_{5,6}$ 8.5 Hz, chlorobenzene H-6), 7.00 (m, 0.4 H, chlorobenzene H-4, 6), 7.28–8.06 (m, 15 H, Ph), 8.57 (s, 0.2 H, isoxazole H-3), 8.58 (s, 0.8 H, isoxazole H-3), 8.70 (s, 0.8 H, –CH=N–), 8.71 (s, 0.2 H, –CH=N–); ^{13}C NMR ($CDCl_3$): δ 63.6, 63.7 (C-5′), 71.6, 72.3, 74.6, 74.9, 75.9, 76.5, 80.9, 81.6 (C-1′, 2′, 3′, 4′), 115.0, 116.3, 117.1, 117.8, 117.9, 118.1 (Ph), 119.6, 122.9 (C-4), 127.9–143.2 (Ph), 146.0, 146.8 (C-3), 149.2, 149.3 (–CH=N–), 165.3, 165.8, 166.1, 166.4, 166.7, 167.0 (C-5, C=O). FABMS (nitrobenzyl alcohol as matrix): Calcd for $C_{36}H_{29}ClN_3O_8$; 666.1643 [MH]. Found: m/z 666.1636 $[MH]^+$.

*7-Chloro-3-cyano-4-(2,3,5-tri-*O*-benzoyl-β-*D*-ribofuranosyl)-1*H*-1,5-benzodiazepine* (**4c**).—To a solution of **1** (65.3 mg, 0.121 mmol) in $CHCl_3$ (11.5 mL) was added 4-chloro-1,2-phenylenediamine (**2c**) (26.9 mg, 0.181 mmol). The mixture was stirred at rt for 2 days, and then the reaction mixture was evaporated. The residue was purified by PTLC with 1.5:1 hexane–EtOAc as eluent to give 51.0 mg (62%) of **4c** as a pale yellow form; IR (KBr) 2208 (CN) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 4.75 (dd, 1 H, $J_{4',5'a}$ 5.1, $J_{5'a,5'b}$ 12.3 Hz, H-5′a), 4.91 (m, 1 H, H-4′), 4.96 (dd, 1 H, $J_{4',5'b}$ 3.3, $J_{5'a,5'b}$ 12.3 Hz, H-5′b), 5.89 (m, 2 H, H-1′, 3′), 6.06 (dd, 1 H, $J_{1',2'} = J_{2',3'}$ 5.1 Hz, H-2′), 7.19–7.68 (m, 12 H, Ph), 7.96–8.86 (m, 6 H, Ph), 8.86 (s, 1 H, H-2), 11.00 (br, 1 H, NH, exchanged with D_2O); ^{13}C NMR ($CDCl_3$): δ 63.3 (C-5′), 71.6 (C-3′), 74.5 (C-2′), 76.4 (C-1′), 81.4 (C-4′), 110.9 (CN), 111.4, 112.1, 119.2, 120.2, 123.5, 124.0 (C-6, 8, 9), 128.4–134.0, 143.0, 144.3 (C-3, Ph), 150.7 (C-2), 163.2 (C-4), 165.3, 165.7, 166.4 (C=O). Anal. Calcd for $C_{36}H_{26}ClN_3O_7 \cdot 1.6\ H_2O$; C, 63.38; H, 4.35; N, 6.21. Found: C, 63.49; H, 3.88; N, 6.12.

General procedure for deprotection.—Sodium methoxide in MeOH (2 mL, 0.75 mmol) was added to the protected *C*-nucleoside (0.05 mmol) dissolved in MeOH (2 mL). The mixture was stirred at −15 °C for 2 h, and then the mixture was neutralized with HOAc and evaporated under reduced pressure. The residue was chromatographed on a column of silica gel with 7:3 $CHCl_3$–MeOH as eluent. The mixture was purified by PTLC to afford the corresponding deprotected free *C*-nucleoside.

*3-Cyano-8-nitro-4-(β-*D*-ribofuranosyl)-1*H*-1,5-benzodiazepine* (**7a**).—Compound **7a**: yellow oil; yield 87%; $[\alpha]_D$ −107.8° (*c* 0.7, CH_3OH); ^{1}H NMR [$(CD_3)_2SO$]: δ 3.35 (br, 2 H, OH, exchanged with D_2O), 3.60 (dd, 1 H, $J_{4',5'a}$ 4.4, $J_{5'a,5'b}$ 11.7 Hz, H-5′a), 3.67 (dd, 1 H, $J_{4',5'b}$ 4.4, $J_{5'a,5'b}$ 11.7 Hz, H-5′b), 3.98 (m, 1 H, H-4′), 4.08 (m, 1 H, H-3′), 4.30 (m, 1 H, H-2′), 5.21 (br, 1 H, OH, exchanged with D_2O), 5.54 (d, 1 H, $J_{1',2'}$ 6.6 Hz, H-1′), 7.80 (d, 1 H, $J_{6,7}$ 8.8 Hz, H-6), 8.15 (dd, 1 H, $J_{6,7}$ 8.8, $J_{7,9}$ 2.2 Hz, H-7), 8.51 (d, 1 H, $J_{7,9}$ 2.2 Hz, H-9), 9.22 (s, 1 H, H-2); ^{13}C NMR (CD_3COCD_3): δ 62.1 (C-5′), 71.7, 76.4, 78.9, 88.1 (C-1′, 2′, 3′, 4′), 109.7 (CN), 112.0, 114.6 (C-6, 9), 118.9 (C-7), 148.2 (C-3), 151.7 (C-2), 169.1 (C-4). FABMS (nitrobenzyl alcohol as matrix): Calcd for $C_{15}H_{15}N_4O_6$; 347.0092 [MH]. Found: m/z 347.1000 $[MH]^+$.

*3-Cyano-7-methoxy-4-(β-*D*-ribofuranosyl)-1*H*-1,5-benzodiazepine* (**7b**).—Compound **7b**: yellow oil; yield 81%; $[\alpha]_D$ −88.3° (*c* 1.1, CH_3OH); ^{1}H NMR [$(CD_3)_2SO$]: δ 3.59 (dd, 1 H, $J_{4',5'a}$ 4.4, $J_{5'a,5'b}$ 10.6 Hz, H-5′a), 3.65 (dd, 1 H, $J_{4',5'b}$ 3.7, $J_{5'a,5'b}$ 10.6 Hz, H-5′b), 3.80 (s, 3 H, OCH_3), 3.95–4.30 (m, 3 H, H-2′, 3′, 4′), 5.51 (d, 1 H, $J_{1',2'}$ 7.3 Hz, H-1′), 6.87 (dd, 1 H, $J_{6,8}$ 2.4, $J_{8,9}$ 8.8 Hz, H-8), 7.11 (s, 1 H, H-6), 7.51 (d, 1 H, $J_{8,9}$ 8.8 Hz, H-9), 9.14 (s, 1 H, H-2); ^{13}C NMR (CD_3COCD_3): δ 55.9, 5 6.1 (OCH_3), 62.4 (C-5′), 72.0, 76.0, 78.6, 88.1 (C-1′, 2′, 3′, 4′), 97.5, 97.9, 112.3, 113.3, 113.7 (C-6, 8, 9), 110.3 (CN), 143.0 (C-3), 151.3 (C-2), 157.7 (C-7), 167.9 (C-4). Calcd for $C_{16}H_{18}N_3O_6$; 348.1196 [MH]. Found: m/z 348.1203 $[MH]^+$.

*7-Chloro-3-cyano-4-(β-*D*-ribofuranosyl)-1*H*-1,5-benzodiazepine* (**7c**).—Compound **7c**: pale yellow solid; yield 51%; $[\alpha]_D$ −95.4° (*c*

0.7, CH_3OH); ^1H NMR [$(CD_3)_2SO$]: δ 3.36 (br, 2 H, OH, exchanged with D_2O), 3.59 (dd, 1 H, $J_{4',5'a}$ 4.4, $J_{5'a,5'b}$ 11.7 Hz, H-5′a), 3.66 (dd, 1 H, $J_{4',5'b}$ 3.7, $J_{5'a,5'b}$ 11.7 Hz, H-5′b), 3.96 (m, 1 H, H-4′), 4.08 (m, 1 H, H-3′), 4.28 (dd, 1 H, $J_{1',2'} = J_{2',3'}$ 6.6 Hz, H-2′), 5.20 (br, 1 H, OH, exchanged with D_2O), 5.52 (d, 1 H, $J_{1',2'}$ 6.6 Hz, H-1′), 7.24 (dd, 1 H, $J_{6,8}$ 1.8, $J_{8,9}$ 8.6 Hz, H-8), 7.64 (d, 1 H, $J_{8,9}$ 8.6 Hz, H-9), 7.69 (s, 1 H, H-6), 9.17 (s, 1 H, H-2), 12.88 (br, 1 H, NH, exchanged with D_2O); ^{13}C NMR [$(CD_3)_2SO$]: δ 61.6 (C-5′), 71.3 (C-3′), 74.5 (C-2′), 75.4 (C-1′), 86.1 (C-4′), 109.7 (CN),111.2, 112.9 (C-9), 118.1, 120.0 (C-6), 122.5, 122.9 (C-8), 126.4, 127.1, 133.0, 135.0, 139.5, 142.1, 144.1 (C-3, 5a, 7, 9a), 150.2 (C-2), 168.0 (C-4). Due to the unstable nature of this compound an acceptable elemental analysis could not be obtained.

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