ELSEVIER

www.elsevier.nl/locate/carres

Carbohydrate Research 329 (2000) 681–686

CARBOHYDRATE RESEARCH

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

Natsu Nishimura, Haruna Hisamitsu, Michiharu Sugiura, Isamu Maeba *

Faculty of Pharmacy, Meijo University, Tempaku, Nagoya 468, Japan

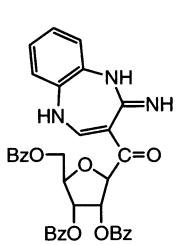
Received 20 June 2000; accepted 29 July 2000

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).



(A)

* Corresponding author. Tel.: +81-52-8321781; fax: +81-52-8348090.

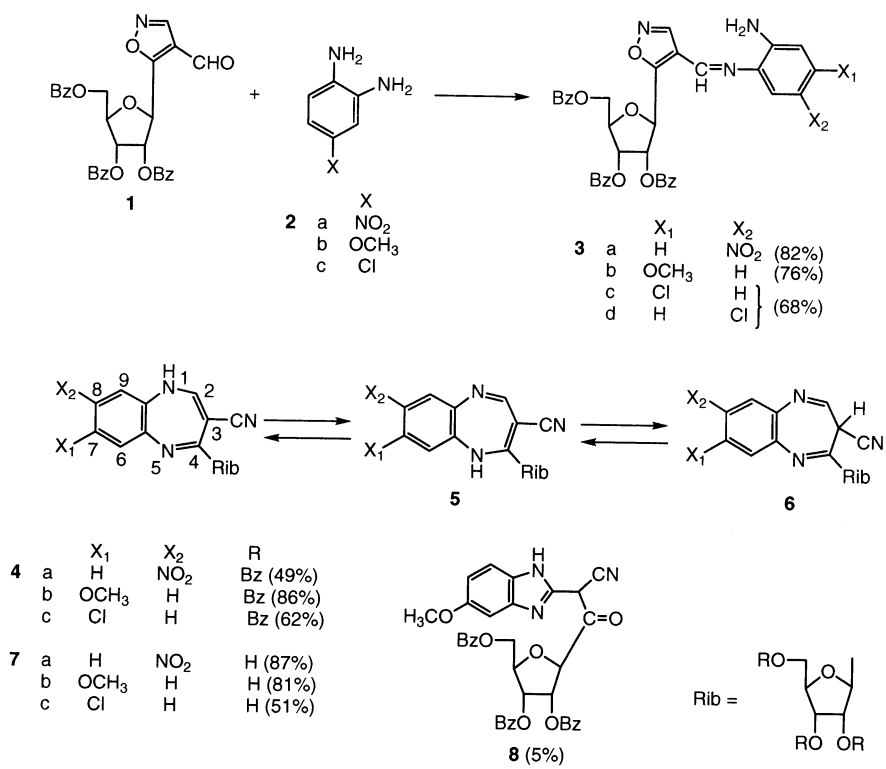
E-mail address: maeba@meijo-u.ac.jp (I. Maeba).

0008-6215/00/$ - see front matter
PII: S0008-6215(00)00231-7

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.

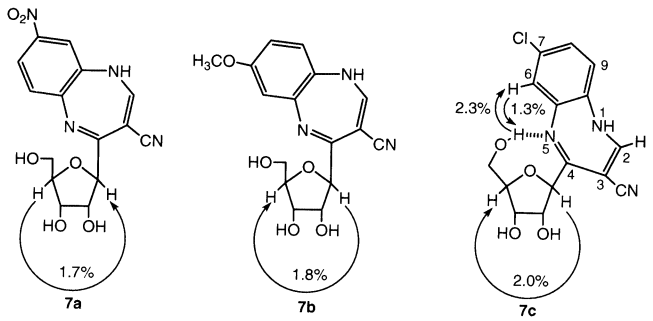


Fig. 1. NOE experiments for compounds **7a**–**c**.

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)-1*H*-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.

Acknowledgements

This work was partly supported by the Ministry of Education Science, Sports and Culture of Japan (High-Tech Research Center Project).

References

[1] Nishimura, N.; Koyano, Y.; Sugiura, M.; Maeba, I. *Heterocycles* 1999, *51*, 803–809.
[2] Nishiyama, Y.; Nishimura, N.; Kuroyanagi, N.; Maeba, I. *Carbohydr. Res.* 1997, *300*, 283–288.
[3] (a) Atta-ur-Rahman, *Nuclear Magnetic Resonance*, Springer-Verlag, New York, 1986, p. 135. (b) Atta-ur-Rahman, S. Malik, H. Cun-heng, J. Clardy, *Tetrahedron Lett.*, 26 (1985) 2759–2762.
[4] Y. Okamoto, T. Ueda, *J. Chem. Soc., Chem. Commun.*, (1973) 367–368.