C-NUCLEOSIDES. 19.[1] SYNTHESIS OF 7- AND 8-SUBSTITUTED 4-[1-(β-D-RIBOFURANOSYL)OXO]-1,3-DIHYDRO-2H-1,5-BENZODIAZEPIN-2-ONE

Yasutaka Ito, Masakazu Wakimura, C. Ito, and Isamu Maeba*
Faculty of Pharmacy, Meijo University, Tempaku-ku, Nagoya 468, Japan

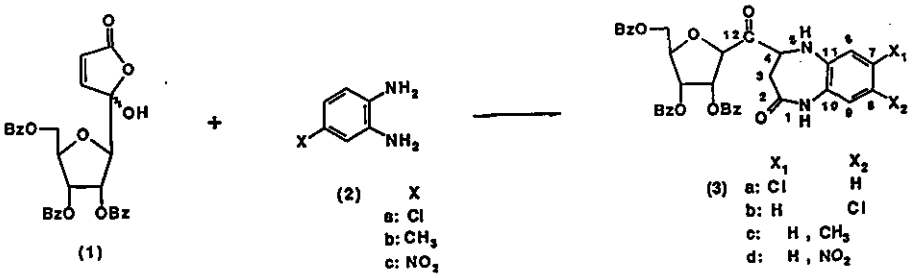
Abstract------- The synthesis of 7- and 8-substituted 4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-one from furanone glycoside (**1**) is described. Treatment of 1,2-diamino-4-substituted benzenes (**2a-c**) with **1** gave a mixture of 7- and 8-substituted 4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3,4,5-tetrahydro-2H-1,5-benzodiazepin-2-one (**3a-d**). Dehydrogenation of **3a-d** with DDQ and a trace of PTSA afforded 7- and 8-substituted 4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-ones (**4a-f**). The position of the substituent in compounds (**4a-f**) was confirmed by ^{1}H-^{13}C long-range COSY and NOE experiments with the corresponding N_1-methyl derivatives (**5a-c**). Deprotection of compounds (**4a-e**) with methanolic sodium hydroxide afforded **4g-k**.

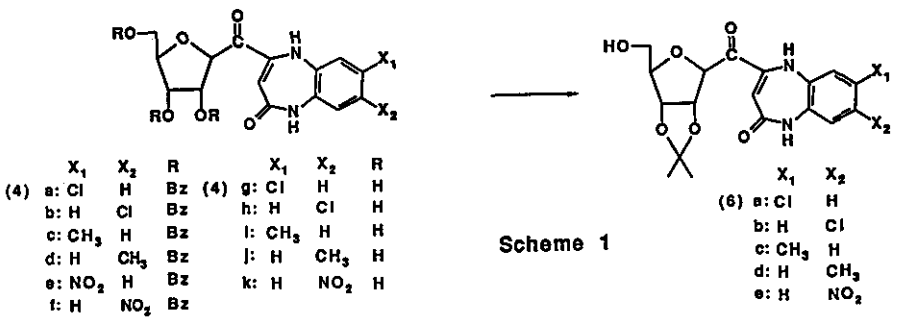
In a recent report[2] from our laboratory, we described the preparation of 4-[1-(β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-one through condensation of 1,2-diaminobenzene with furanone glycoside (**1**). It was of interest to examine whether 7-substituted benzodiazepin-2-one homo-C-nucleosides or the corresponding 8-isomers would be obtained on treatment of 1,2-diamino-4-substituted benzenes with compound (**1**).

Treatment of 1,2-diamino-4-chlorobenzene (**2a**) with furanone glycoside (**1**) in chloroform at room temperature gave a mixture of 7- and 8-chloro-4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3,4,5-tetrahydro-2H-1,5-benzodiazepin-2-ones (**3a**) and (**3b**) in 20% and 34% yield, respectively (Scheme 1). Compound (**3b**) was faster moving on tlc than was its isomer **3a**. Compounds (**3a**) and (**3b**) are an inseparable mixture of diastereoisomers (differing in configuration only at C-4). The ^{1}H nmr spectra of **3a** and **3b** show that, in the higher field region, a couple of 3-CH_2-4-CH- protons resonate as an ABX system.[3] While compounds (**3a**) and (**3b**) gave satisfactory ^{1}H and ^{13}C nmr spectra, it appeared to be unstable. Dehydrogenation of **3a** and **3b** with 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) and a trace of p-toluenesulfonic acid (PTSA) in chloroform at room

temperature afforded 7- and 8-chloro-4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-ones (**4a**) and (**4b**) in 11% and 22% yield, respectively. The position of the substituent in compound (**4b**) was determined by ^{1}H-^{13}C long-range COSY and NOE experiments with the correponding N_1-methyl derivative (**5a**), prepared by methylation of **4b** with methyl iodide. In the ^{1}H-^{13}C long-range experiment of **5a**, a correlation was obserbed between methyl proton at δ 3.57 and C-2 at δ 155.23. Irradiation of the methyl signal in **5a** gave a 12 % enhancement of the signal at δ 7.16 showing as a singlet. This data indicated that the chloro group in **4b** was located at the 8 position. Therefore, the position of the chloro group in compound (**4a**) was assigned at the C-7.

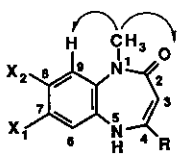
When the same reaction of furanone glycoside (**1**) with 1,2-diamino-4-methylbenzene (**2b**) is performed, an inseparable mixture of 7- and 8-methyl-4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3,4,5-tetrahydro-2H-1,5-benzodiazepin-2-one (**3c**) is obtained in 40% yield. Compound (**3c**) was dehydrogenated with DDQ and a trace of PTSA to afford 7- and 8-methyl-4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-ones (**4c**) and (**4d**) which could be separated by preparative tlc. Next, furanone glycoside (**1**) and 1,2-diamino-4-nitrobenzene (**2c**) in toluene were heated at 90 °C for 5 h giving a 91% yield of an inseparable mixture of 7- and 8-nitro-4-[1-2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3,4,5-tetrahydro-2H-





Scheme 1

1,5-benzodiazepin-2-ones (**3d**). Compound (**3d**) was also successfully dehydrogenated by the same procedure afford 7- and 8-nitro-4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-ones (**4e**) and (**4f**) which could be separated by preparative tlc. The positions of the substituent in **4c-f** were also determined by ^{1}H-^{13}C long-range COSY and NOE experiments with the corresponding N_1-methyl derivatives (**5b,c**)(Figure 1). Debenzoylation of compounds (**4a-e**) with methanolic sodium hydroxide afforded the deblocked compounds (**4g-k**). However, the removal of the sugar protecting groups in **4f** with alkaline did not afford the deprotected 7-nitro-1,5-benzodiazepin-2-one homo-C-nucleoside. The assignments of anomeric configuration of compounds (**4g-k**) were made on the basis of the difference in the chemical shifts of the two methyl signals of the corresponding 2,3-O-isopropylidene derivatives (**6a-e**). The ^{1}H nmr chemical-shift differential value ($\Delta\delta$) of the methyl groups in the isopropylidene derivatives is indicative of β stereochemistry in accordance with the Imbach's rule[4] (<0.15 and >0.15 ppm for the α and β anomers)(see Experimental). This showed that the β-ribofuranoside configuration had been preserved during the reaction sequence.



	X_1	X_2	NOE enhancement (%)
(5) a:	H	Cl	17.2
b:	CH_3	H	14.0
c:	NO_2	H	12.5

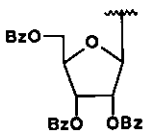


Figure 1 : The ^{1}H -^{13}C long range COSY and NOE experiments with N_1 - metyl compounds (5a - c).

EXPERIMENTAL

Mass spectra were taken on a Hitachi M-80 instrument by direct insertion at 70 eV; fast-atom bombardment (fab) mass spectra were run on a JMS-HX 110. ^{1}H- and ^{13}C-Nmr spectra were measured with a JNM-GX-270 and a GX-400 (JEOL) spectrometers, with tetramethylsilane as internal standard. Analytical tlc was performed on glass plates coated with a 0.5 mm layer of silica gel GF_{254} (Merck). The compounds were detected by uv light (254 nm).

7- and 8-Chloro-4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3,4,5-tetrahydro-2H-1,5-benzodiazepin-2-ones (3a) and (3b). To a solution of **1** (67.6 mg, 0.12 mmol) in chloroform (3 ml) at 0 °C was added 26.6 mg (0.15 mmol) of 4-methyl-1,2-diaminobenzene. The mixture was stirred at room temperature for 5 h, then evaporated, and the residue was separated by plc with hexane-ethyl

acetate (1:1) as developer.

Compound 3a: yield 19.8%; Rf 0.25 (hexane-ethyl acetate, 1:1); ^{1}H nmr ($CDCl_3$) δ 3.01, 3.17 (1 H, each dd, J=9.4 and 18.5 Hz, 3-Ha), 3.49, 3.56 (1 H, each dd, J=3.0 and 18.5 Hz, 3-Hb), 4.42, 4.48 (1 H, each dd, J=3.0 and 9.4 Hz, 4-H), 4.58-4.82 (5 H, m, 1'-, 4'-, 5'-H and NH exchanges with D_2O), 5.73 (1 H, t, J=5.4 Hz, 3'-H), 5.84 (1 H, t, J=5.4 Hz, 2'-H), 6.21-6.71 (3 H, m, 6-, 8- and 9-H), 7.26-8.12 (15 H, m, ArH), 9.38, 9.42 (1 H, br, NH exchanges with D_2O); ^{13}C nmr ($CDCl_3$) δ 41.24, 41.48 (C-3), 51.31, 51.66 (C-4), 63.77 (C-5'), 72.43, 72.72, 73.07, 78.69, 84.89, 85.06 (C-1', -2', -3' and -4'), 107.29-133.85 (Ar-C), 165.33, 165.50, 166.03, 166.15, 168.08 (C=O and C-2), 205.64, 206.11 (C-12). Hrms Found: m/z 424.0832. Calcd for $C_{22}H_{17}N_2O_5Cl$; M^+-2xBzOH, 424.0825.

Compound 3b: yield 33.8%; Rf 0.32 (hexane-ethyl acetate, 1:1); ^{1}H nmr ($CDCl_3$) δ 3.02, 3.18 (1 H, each dd, J=9.4 and 18.5 Hz, 3-Ha), 3.50, 3.59 (1 H, each dd, J=3.0 and 18.5 Hz, 3-Hb), 4.38, 4.45 (1 H, each dd, J=3.0 and 9.4 Hz, 4-H), 4.48-4.79 (5 H, m, 1'-, 4'-, 5'-H and NH exchanges with D_2O), 5.73 (1 H, m, 3'-H), 5.84 (1 H, m, 2'-H), 6.54-6.85 (3 H, m, 6-, 7- and 9-H), 7.26-8.12 (15 H, m, ArH), 9.03 (1 H, br, NH exchanges with D_2O); ^{13}C nmr ($CDCl_3$) δ 41.19 (C-3), 52.18 (C-4), 63.94 (C-5'), 72.60, 72.89, 73.30, 85.30 (C-1', -2', -3' and -4'), 115.66-133.50 (Ar-C), 165.33, 165.50, 166.27, 168.08 (C=O and C-2), 205.87, 206.28 (C-12). Hrms Found: m/z 424.0811. Calcd for $C_{22}H_{17}N_2O_5Cl$; M^+-2xBzOH, 424.0825.

7- and 8-Methyl-4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3,4,5-tetrahydro-2H-1,5-benzodiazepin-2-ones (3c). The same procedure was used as for the reaction of **1** with 4-methyl-1,2-diaminobenzene.

Compound 3c: 39.5%; ^{1}H nmr ($CDCl_3$) δ 2.23, 2.24 (3 H, each s, CH_3), 3.02, 3.20 (1 H, each dd, J=9.4 and 18.5 Hz, 3-Ha), 3.51, 3.58 (1 H, each dd, J=3.0 and 18.5 Hz, 3-Hb), 4.42 (1 H, m, 4-H), 4.60-4.78 (5 H, m, 1'-, 4'-, 5'-H and NH exchanges with D_2O), 5.71 (1 H, m, 3'-H), 5.85 (1 H, m, 2'-H), 6.46-6.72 (3 H, m, 6-, 9-, 7- or 8-H), 7.32-8.13 (15 H, m, ArH), 9.00, 9.04 (1 H, br, NH exchanges with D_2O). Hrms Found: m/z 404.1346. Calcd for $C_{23}H_{20}N_2O_5$; M^+-2xBzOH, 404.1370.

7- and 8-Nitro-4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3,4,5-tetrahydro-2H-1,5-benzodiazepin-2-ones (3d). To a solution of **1** (20.0 mg, 0.04 mmol) in toluene (2 ml) was added 6.8 mg (0.04 mmol) of 4-nitro-1,2-diaminobenzene. The mixture was heated at 90 °C for 5 h, then evaporated under reduced pressure, and the residue was purified by plc with hexane-ethyl acetate (1:1) as developer.

Compound 3d: yield 91.3%; ^{1}H nmr ($CDCl_3$) δ 3.18 (1 H, m, 3-Ha), 3.55 (1 H, m, 3-Hb), 4.47-87 (6 H,

m, 1'-, 4'-, 5'-, 4-H and NH exchanges with D_2O), 5.76 (1 H, m, 3'-H), 5.86 (1 H, m, 2'-H), 6.74 (1 H, m, 6- or 9-H), 7.28-8.07 (17 H, m, ArH), 9.29, 9.32 (1 H, br, NH exchanges with D_2O). Hrms Found: m/z 435.1091. Calcd for $C_{22}H_{17}N_3O_7$; M^+-2xBzOH, 435.1065.

7- and 8-Chloro-4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-ones (4a) and (4b). To a solution of 1 (100 mg, 0.18 mmol) in chloroform (3 ml) at 0 °C was added 39.4 mg (0.28 mmol) of 4-chloro-1,2-diaminobenzene. The mixture was stirred at room temperature for 5 h. After the tlc analysis indicated complete disappearance of starting material, DDQ (83.5 mg, 0.36 mmol) and PTSA (15 mg) were added, and the mixture was stirred for additional 1.5 h. Water was added, and the mixture was extracted with chloroform. The extracts were combined, washed with water, and dried over magnesium sulfate. The extracts, on evaporation, afforded a yellow oil which was separated by plc with chloroform-methanol (200:1) as developer.

Compound 4a: yield 11.2%; Rf 0.48 (hexane-ethyl acetate, 1:1); ^1H nmr ($CDCl_3$) δ 4.62 (1 H, dd, J=4.0 and 12.1 Hz, 5'-Ha), 4.78 (1 H, m, 4'-H), 4.91 (1 H, d, J=4.0 Hz, 1'-H), 4.94 (1 H, m, 5'-Hb), 5.78 (1 H, dd, J=5.0 and 6.4 Hz, 3'-H), 6.00 (1 H, dd, J=4.0 and 5.0 Hz, 2'-H), 6.68 (1 H, s, 3-H), 6.99-7.11 (3 H, m, 6-, 8- and 9-H), 7.26-8.05 (15 H, m, ArH), 11.15, 13.24 (2 H, each br s, NH exchanges with D_2O); ^{13}C nmr ($CDCl_3$) δ 63.94 (C-5'), 72.54, 74.71, 80.03, 85.18 (C-1', -2', -3' and -4'), 91.09 (C-3), 117.24-133.44 (Ar-C), 144.91 (C-4), 157.02 (C-2), 165.33 (C=O), 195.69 (C-12). Hrms Found: m/z 422.0701. Calcd for $C_{22}H_{15}N_2O_5Cl$; M^+-2xBzOH, 422.0668.

Compound 4b: yield 22.6%; Rf 0.56 (hexane-ethyl acetate, 1:1); ^1H nmr ($CDCl_3$) δ 4.64 (1 H, dd, J=4.0 and 11.8 Hz, 5'-Ha), 4.79 (1 H, m, 4'-H), 4.88 (1 H, m, 5'-Hb), 4.92 (1 H, d, J=3.7 Hz, 1'-H), 5.78 (1 H, t, J=3.7 Hz, 3'-H), 6.01 (1 H, t, J=3.7 Hz, 2'-H), 6.68 (1 H, s, 3-H), 7.02-7.25 (3 H, m, 6-, 7- and 9-H), 7.26-8.04 (15 H, m, ArH), 11.07, 13.38 (2 H, each br s, NH exchanges with D_2O); ^{13}C nmr ($CDCl_3$) δ 64.12 (C-5'), 72.72, 74.86, 80.03, 85.24 (C-1', -2', -3' and -4'), 90.85 (C-3), 123.09-133.39 (Ar-C), 144.97 (C-4), 156.85 (C-2), 165.39, 166.15 (C=O), 195.11 (C-12). Hrms Found: m/z 424.0687. Calcd for $C_{22}H_{15}N_2O_5Cl$; M^+-2xBzOH, 422.0668.

7- and 8-Methyl-4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-ones (4c) and (4d). The same procedure was used as for the reaction of 1 with 4-chloro-1,2-diaminobenzene.

Compound 4c: yield 18%; Rf 0.44 (chloroform-methanol, 97:3); ^1H nmr ($CDCl_3$) δ 2.37 (3 H, s, CH_3), 4.65 (1 H, dd, J=4.4 and 11.8 Hz, 5'-Ha), 4.77 (1 H, m, 4'-H), 4.87 (1 H, m, 5'-Hb), 4.91 (1 H, d,

J=4.0 Hz, 1'-H), 5.78 (1 H, dd, J=5.0 and 6.4 Hz, 3'-H), 5.99 (1 H, dd, J=4.0 and 5.0 Hz, 2'-H), 6.65 (1 H, s, 3-H), 6.96 (3 H, m, 6-, 8- and 9-H), 7.29-8.10 (15 H, m, ArH), 10.69, 13.44 (2 H, each br s, NH exchanges with D_2O); ^{13}C nmr ($CDCl_3$) δ 21.03 (CH_3), 64.00 (C-5'), 72.43, 74.74, 79.72, 85.10 (C-1', -2', -3' and -4'), 90.11 (C-3), 115.94, 116.44, 125.68 (C-6, -8 and -9), 123.72, 124.13 (C-10 and -11), 128.19-134.94 (Ar-C), 145.54 (C-4), 157.13 (C-2), 165.27, 166.25 (C=O), 194.68 (C-12). Hrms Found: m/z 402.1243. Calcd for $C_{23}H_{18}N_2O_5$; M^+-2xBzOH, 402.1214.

Compound 4d: yield 23.1%, Rf 0.48 (chloroform-methanol, 97:3); ^1H nmr ($CDCl_3$) δ 2.38 (3 H, s, CH_3), 4.65 (1 H, dd, J=4.4 and 11.8 Hz, 5'-Ha), 4.77 (1 H, m, 4'-H), 4.87 (1 H, m, 5'-Hb), 4.91 (1 H, d, J=4.0 Hz, 1'-H), 5.77 (1 H, t, J=4.0 Hz, 3'-H), 5.99 (1 H, t, J=4.0 Hz, 2'-H), 6.64 (1 H, s, 3-H), 6.92-7.08 (3 H, m, 6-, 7- and 9-H), 7.29-8.13 (15 H, m, ArH), 10.95, 13.58 (2 H, each br s, NH exchanges with D_2O); ^{13}C nmr ($CDCl_3$) δ 21.03 (CH_3), 63.88 (C-5'), 72.34, 74.78, 79.66, 85.09 (C-1', -2', -3' and -4'), 89.76 (C-3), 116.22, 116.32, 125.85 (C-6, -7 and -9), 122.09 (C-10 or -11), 128.14-135.25 (Ar-C), 145.50 (C-4), 157.41 (C-2), 165.27, 166.22 (C=O), 194.07 (C-12). Hrms Found: m/z 402.1223. Calcd for $C_{23}H_{18}N_2O_5$; M^+-2xBzOH, 402.1214.

7- and 8-Nitro-4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-ones (4e) and (4f). To a solution of 1 (100.0 mg, 0.18 mmol) in toluene (3 ml) was added 6.8 mg (0.04 mmol) of 4-nitro-1,2-diaminobenzene. The mixture was heated at 90 °C for 5 h, then evaporated under reduced pressure. Then, chloroform (3 ml), DDQ (83.5 mg, 0.36 mmol) and PTSA (15 mg) were added, and the mixture was stirred at room temperature for 30 min. Water was added, and the mixture was extracted with chloroform (3X10 ml). The extracts were combined, washed with water, and dried over magnesium sulfate. The extracts, on evaporation, afforded a yellow oil which was separated by plc with chloroform-methanol (200:1) as developer.

Compound 4e: yield 19.9%; Rf 0.36 (chloroform-methanol, 97:3); ^1H nmr ($CDCl_3$) δ 4.61 (1 H, dd, J=4.0 and 12.1 Hz, 5'-Ha), 4.80 (1 H, m, 4'-H), 4.93 (1 H, d, J=4.0 Hz, 1'-H), 4.96 (1 H, m, 5'-Hb), 5.79 (1 H, t, J=4.0 Hz, 3'-H), 6.02 (1 H, t, J=4.0 Hz, 2'-H), 6.73 (1 H, s, 3-H), 7.17-8.04 (18 H, m, Ar-H), 11.42, 13.11 (2 H, each br s, NH exchanges with D_2O); ^{13}C nmr ($CDCl_3$) δ 63.78 (C-5'), 72.34, 74.48, 79.96, 85.09 (C-1', -2', -3' and -4'), 91.96 (C-3), 111.81, 116.32, 119.56 (C-6, -8 and -9), 124.48 (C-10 or -11), 128.24-133.56 (Ar-C), 143.96 (C-4), 157.32 (C-2), 165.36, 166.13 (C=O), 196.52 (C-12). Hrms Found: m/z 433.0918. Calcd for $C_{22}H_{15}N_3O_7$; M^+-2xBzOH, 433.0909.

Compound 4f: yield 22%; Rf 0.40 (chloroform-methanol, 97:3); ^1H nmr ($CDCl_3$) δ 4.61 (1 H, dd, J=4.0 and 12.1 Hz, 5'-Ha), 4.79 (1 H, m, 4'-H), 4.90 (1 H, m, 5'-Hb), 4.93 (1 H, d, J=4.0 Hz, 1'-H), 5.76 (1 H, t, J=4.0 Hz, 3'-H), 6.01 (1 H, t, J=4.0 Hz, 2'-H), 6.78 (1 H, s, 3-H), 7.15-8.13 (19 H,

m, Ar-H and NH exchanges with D_2O), 13.05 (1 H, br s, NH exchandes with D_2O); ^{13}C nmr ($CDCl_3$) δ 63.75 (C-5'), 72.33, 74.30, 79.98, 85.12 (C-1', -2', -3' and -4'), 93.29 (C-3), 111.81, 115.98, 120.22 (C-6, -7 and -9), 125.66 (C-10 or -11), 128.20-133.53 (Ar-C), 143.23 (C-4), 156.75 (C-2), 165.35, 166.15 (C=O), 197.22 (C-12). Hrms Found: m/z 433.0919. Calcd for $C_{22}H_{15}N_3O_7$; M^+-2xBzOH, 433.0909.

General Deprotection Procedure. Sufficient methanolic sodium hydroxide (0.5 ml, 0.63 mmol) was added to the protected C-nucleoside (0.07 mmol) in methanol(4 ml). The mixture was kept at room temperature for 5 h, rendered neutral with acetic acid, and evaporated. The residue was purified by plc to afford the free C-nucleoside.

7-Chloro-4-[1-(β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-one (4g): mp 168-169°C; yield 20.1%; ^1H nmr (CD_3OD) δ 3.69 (1 H, dd, J=2.0 and 12.4 Hz, 5'-Ha), 3.83 (1 H, dd, J=2.4 and 12.4 Hz, 5'-Hb), 3.98 (2 H, m, 3'- and 4'-H), 4.12 (1 H, t, J=4.7 Hz, 2'-H), 4.39 (1 H, d, J=4.7 Hz, 1'-H), 6.48 (1 H, s, 3-H), 7.05-7.15 (2 H, m, 8- and 9-H), 7.39 (1 H, d, J=1.7 Hz, 6-H); ^{13}C nmr [$(CD_3)_2SO$] δ 62.04 (C-5'), 71.41, 74.62, 84.28, 86.91 (C-1', -2', -3' and -4'), 90.38 (C-3), 115.98, 116.59, 123.29, 125.39, 125.51, 127.17 (C-6, -7, -8, -9, -10 and -11), 144.03 (C-4), 155.47 (C-2), 198.43 (C-12). Hrms Found: m/z 318.0382. Calcd for $C_{15}H_{11}N_2O_4Cl$; M^+-2xH_2O, 318.0405.

8-Chloro-4-[1-(β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-one (4h): mp 211-213°C; yield 13.7%; ^1H nmr (CD_3OD) δ 3.69 (1 H, dd, J=2.0 and 10.8 Hz, 5'-Ha), 3.83 (1 H, dd, J=2.0 and 10.8 Hz, 5'-Hb), 3.97 (2 H, m, 3'- and 4'-H), 4.11 (1 H, t, J=4.7 Hz, 2'-H), 4.39 (1 H, d, J=4.7 Hz, 1'-H), 6.46 (1 H, s, 3-H), 7.14 (2 H, m, 7- and 9-H), 7.28 (1 H, d, J=9.4 Hz, 6-H); ^{13}C nmr [$(CD_3)_2SO$] δ 62.08 (C-5'), 71.45, 74.70, 84.29, 86.89 (C-1', -2', -3' and -4'), 90.00 (C-3), 114.67, 117.98, 123.19, 123.34, 127.28, 127.89 (C-6, -7, -8, -9, -10 and -11), 144.21 (C-4), 155.66 (C-2), 208.16 (C-12). Hrms Found: m/z 318.0429. Calcd for $C_{15}H_{11}N_2O_4Cl$; M^+-2xH_2O, 318.0405.

7-Methyl-4-[1-(β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-one (4i): mp 210-212°C; yield 26.8%; ^1H nmr (CD_3OD) δ 2.36 (3 H, s, CH_3), 3.67 (1 H, m, 5'-Ha), 3.84 (1 H, dd, J=2.7 and 12.4 Hz, 5'-Hb), 3.98 (2 H, m, 3'- and 4'-H), 4.11 (1 H, t, J=4.4 Hz, 2'-H), 4.39 (1 H, d, J=4.4 Hz, 1'-H), 6.43 (1 H, s, 3-H), 7.02 (2 H, m, 8-, and 9-H), 7.12 (1 H, s, 6-H); ^{13}C nmr [$(CD_3)_2SO$] δ 20.53 (CH_3), 62.09 (C-5'), 71.42, 74.73, 84.22, 86.92 (C-1', -2', -3' and -4'), 89.39 (C-3), 115.24, 116.34, 124.36 (C-6, -8 and -9), 123.80, 124.81, 133.16 (C-7, -10 and -11), 144.98 (C-4), 155.40 (C-2), 198.03 (C-12). Hrms Found: m/z 298.0942. Calcd for $C_{16}H_{14}N_2O_4$; M^+-2xH_2O, 298.0952.

8-Methyl-4-[1-(β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-one (4j): mp 165-167°C; yield 25.9%; ^1H nmr (CD_3OD) δ 2.35 (3 H, s, CH_3), 3.69 (1 H, m, 5'-Ha), 3.86 (1 H, m, 5'-Hb), 3.98

(2 H, m, 3'- and 4'-H), 4.11 (1 H, t, J=4.4 Hz, 2'-H), 4.39 (1 H, d, J=4.4 Hz, 1'-H), 6.40 (1 H, s, 3-H), 6.99 (2 H, m, 7- and 9-H), 7.18 (1 H, d, J=8.1 Hz, 6-H); ^{13}C nmr [$(CD_3)_2SO$] δ 20.67 (CH_3), 62.12 (C-5'), 71.43, 74.75, 84.19, 86.85 (C-1', -2', -3' and -4'), 89.02 (C-3), 115.38, 116.33, 124.50 (C-6, -7 and -9), 121.83, 126.59, 133.57 (C-8, -10 and -11), 144.88 (C-4), 155.66 (C-2), 197.48 (C-12). Hrms Found: m/z 298.0939. Calcd for $C_{16}H_{14}N_2O_4$; M^+-2xH_2O, 298.0952.

8-Nitro-4-[1-(β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-one (4k): mp 210-212°C; yield 12.7%; ^{1}H nmr (CD_3OD) δ 3.69 (1 H, dd, J=4.0 and 11.8 Hz, 5'-Ha), 3.80 (1 H, dd, J=3.0 and 11.8 Hz, 5'-Hb), 3.98 (2 H, m, 3'- and 4'-H), 4.13 (1 H, t, J=4.7 Hz, 2'-H), 4.41 (1 H, d, J=4.7 Hz, 1'-H), 6.59 (1 H, s, 3-H), 7.42 (1 H, d, J=9.1 Hz, 6-H), 7.95 (1 H, d, J=2.0 Hz, 9-H), 8.01 (1 H, dd, J=9.1 and 2.0 Hz, 7-H); ^{13}C nmr [$(CD_3)_2SO$] δ 61.99 (C-5'), 71.46, 74.57, 84.51, 86.98 (C-1', -2', -3' and -4'), 92.42 (C-3), 110.43, 116.58, 118.99 (C-6, -7 and -9), 126.75, 130.20 (C-10 and -11), 142.05, 142.98 (C-4 and -8), 155.68 (C-2), 199.68 (C-12). Hrms Found: m/z 329.0636. Calcd for $C_{15}H_{11}N_3O_6$; M^+-2xH_2O, 329.0646.

General Methylation Procedure. To a solution of a protected C-nucleoside (0.05 mmol) in acetone (3 ml) was added methyl iodide (130 mg, 0.9 mmol) and potassium carbonate (175 mg, 1.1 mmol) and the mixture was refluxed for 5 h, then evaporated. Water was added, and the mixture was extracted with chloroform. The extracts were combined, washed with water and dried over magnesium sulfate. The extracts, on evaporation, afforded a syrup, which was purified by plc with chloroform as developer.

8-Chlorolo-1-methyl-4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-one (5a): yield 54.5%; ^{1}H nmr ($CDCl_3$) δ 3.57 (3 H, s, CH_3), 4.63 (1 H, dd, J=4.4 and 11.8 Hz, 5'-Ha), 4.76 (1 H, m, 4'-H), 4.85 (1 H, dd, J=3.7 and 11.8 Hz, 5'-Hb), 4.89 (1 H, d, J=4.0 Hz, 1'-H), 5.74 (1 H, dd, J=5.4 and 6.4 Hz, 3'-H), 5.97 (1 H, dd, J=4.0 and 5.4 Hz, 2'-H), 6.66 (1 H, s, 3-H), 7.07 (1 H, d, J=8.7 Hz, 6-H), 7.16 (2 H, apparent d, 7- and 9-H), 7.26-8.07 (15 H, m, ArH), 13.54 (1 H, br s, NH exchanges with D_2O); ^{13}C nmr ($CDCl_3$) δ 29.86 (N-CH_3), 64.04 (C-5'), 72.45, 74.55, 79.68, 85.09 (C-1', -2', -3' and -4'), 91.28 (C-3), 114.56, 117.74, 124.25 (C-6, -7 and -9), 123.41, 128.14-133.38 (C-8, -10, -11 and Ar-C), 144.59 (C-4), 155.23 (C-2), 165.21, 165.25, 166.14 (C=O), 194.72 (C-12). Hrms Found: m/z 436.0802. Calcd for $C_{23}H_{17}N_2O_5Cl$; M^+-2xBzOH, 436.0824.

1,7-Dimethyl-4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-one (5b): yield 76.1%; ^{1}H nmr ($CDCl_3$) δ 2.38, 3.59 (6 H, each s, CH_3), 4.66 (1 H, dd, J=4.4 and 11.7 Hz, 5'-Ha), 4.75 (1 H, m, 4'-H), 4.84 (1 H, dd, J=3.9 and 11.7 Hz, 5'-Hb), 4.91 (1 H, d,

J=3.4 Hz, 1'-H), 5.76 (1 H, dd, J=4.9 and 6.8 Hz, 3'-H), 5.97 (1 H, dd, J=3.4 and 4.9 Hz, 2'-H), 6.64 (1 H, s, 3-H), 6.96 (1 H, s, 6-H), 6.99-7.08 (2 H, m, 8- and 9-H), 7.30-8.07 (15 H, m, ArH), 13.58 (1 H, br s, NH exchanges with D_2O); ^{13}C nmr ($CDCl_3$) δ 20.72 (CH_3), 29.75 (N-CH_3), 64.32 (C-5'), 72.60, 74.71, 79.68, 85.20 (C-1', -2', -3' and -4'), 90.72 (C-3), 114.24 (C-9), 117.16, 125.50 (C-6 and -8), 124.51 (C-11), 126.49 (C-10), 128.16-133.33 (Ar-C), 134.47 (C-7), 145.29 (C-4), 155.34 (C-2), 165.24, 165.26, 166.23 (C=O), 194.42 (C-12). Hrms Found: m/z 416.1349. Calcd for $C_{24}H_{20}N_2O_5$; M^+-2xBzOH, 416.1370.

1-Methyl-7-nitro-4-[1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-one (5c): yield 74.6%; ^1H nmr ($CDCl_3$) δ 3.63 (3 H, s, CH_3), 4.59 (1 H, dd, J=3.9 and 12.2 Hz, 5'-Ha), 4.76 (1 H, m, 4'-H), 4.87 (1 H, m, 5'-Hb), 4.90 (1 H, d, J=3.4 Hz, 1'-H), 5.75 (1 H, t, J=3.4 Hz, 3'-H), 5.96 (1 H, t, J=3.4 Hz, 2'-H), 6.72 (1 H, s, 3-H), 7.24 (1 H, d, J=8.8 Hz, 9-H), 7.31-8.06 (17 H, m, ArH), 13.33 (1 H, br s, NH exchanges with D_2O); ^{13}C nmr ($CDCl_3$) δ 30.21 (N-CH_3), 63.78 (C-5'), 72.40, 74.38, 79.99, 85.04 (C-1', -2', -3' and -4'), 92.58 (C-3), 111.79, 114.54, 119.21 (C-6, -8 and -9), 125.08-133.43 (C-10, -11 and Ar-C), 143.68, 143.89 (C-4 and -7), 155.40 (C-2), 165.21, 165.26, 166.08 (C=O), 196.11 (C-12). Hrms Found: m/z 447.1057. Calcd for $C_{23}H_{17}N_3O_7$; M^+-2xBzOH, 447.1064.

General Acetonization Procedure. To a solution of a deprotected C-nucleoside (0.01 mmol) in acetone (2 ml) was added PTSA (5 mg), and the mixture was stirred at room temperature for 2 h. The reaction mixture was neutralized with saturated sodium hydrogen carbonate solution. Water was added, and the mixture was extracted with chloroform. The extracts were combined, washed with water and dried over magnesium sulfate. The extracts, on evaporation, afforded a syrup, which was purified by plc with chloroform-methanol (97:3) as developer.

7-Chloro-4-[1-(2,3-O-isopropylidene-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-one (6a): yield 24.6%; ^1H nmr ($CDCl_3$) δ 1.37, 1.60 (6 H, each s, isopropylidene Me), 3.63 (1 H, m, 5'-Ha), 3.96 (1 H, m, 5'-Hb), 4.44 (1 H, m, 4'-H), 4.78 (4 H, m, 1'-, 2'-, 3'-H and OH exchanges with D_2O), 6.44 (1 H, s, 3-H), 7.00 (1 H, d, J=8.7 Hz, 9-H), 7.12 (1 H, dd, J=2.0 and 8.7 Hz, 8-H), 7.20 (1 H, d, J=2.0 Hz, 6-H), 9.70, 13.12 (2 H, each br s, NH exchanges with D_2O). Hrms Found: m/z 394.0933. Calcd for $C_{18}H_{19}N_2O_6Cl$; M^+, 394.0930.

8-Chloro-4-[1-(2,3-O-isopropylidene-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-one (6b): yield 30%; ^1H nmr ($CDCl_3$) δ 1.37, 1.61 (6 H, each s, isopropylidene Me), 3.62 (1 H, m, 5'-Ha), 3.95 (1 H, m, 5'-Hb), 4.44 (1 H, m, 4'-H), 4.78 (4 H, m, 1'-, 2'-, 3'-H and OH exchanges with D_2O), 6.42 (1 H, s, 3-H), 7.13 (3 H, m, 6-, 7- and 9-H), 9.87, 13.26 (2 H, each br s, NH exchanges

with D_2O). Hrms Found: m/z 394.0943. Calcd for $C_{18}H_{19}N_2O_6Cl$; M^+, 394.0930.

7-Methyl-4-[1-(2,3-O-isopropylidene-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-one (6c): yield 40.0%; ^1H nmr ($CDCl_3$) δ 1.37, 1.61 (6 H, each s, isopropylidene Me), 2.38 (3 H, s, CH_3), 3.63 (1 H, dd, J=3.4 and 12.4 Hz, 5'-Ha), 3.53-3.83 (1 H, br, OH exchanges with D_2O), 3.96 (1 H, dd, J=2.7 and 12.4 Hz, 5'-Hb), 4.44 (1 H, br s, 4'-H), 4.78 (3 H, m, 1'-, 2'- and 3'-H), 6.39 (1 H, s, 3-H), 7.03 (3 H, m, 6-, 8- and 9-H), 10.78, 13.30 (2 H, each br s, NH exchanges with D_2O). Hrms Found: m/z 374.1467. Calcd for $C_{19}H_{22}N_2O_6$; M^+, 374.1475.

8-Methyl-4-[1-(2,3-O-isopropylidene-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-one (6d): yield 43%; ^1H nmr ($CDCl_3$) δ 1.37, 1.61 (6 H, each s, isopropylidene Me), 2.41 (3 H, s, CH_3), 3.63 (1 H, m, 5'-Ha), 3.96 (1 H, m, 5'-Hb), 4.45 (1 H, m, 4'-H), 4.65 (1 H, br s, OH exchanges with D_2O), 4.81 (3 H, m, 1'-, 2'- and 3'-H), 6.39 (1 H, s, 3-H), 6.97-7.17 (3 H, m, 6-, 7- and 9-H), 10.88, 13.44 (2 H, each br s, NH exchanges with D_2O). Hrms Found: m/z 374.1477. Calcd for $C_{19}H_{22}N_2O_6$; M^+, 374.1475.

8-Nitro-4-[1-(2,3-O-isopropylidene-β-D-ribofuranosyl)oxo]-1,3-dihydro-2H-1,5-benzodiazepin-2-one (6e): yield 66.9%; ^1H nmr ($CDCl_3$) δ 1.37, 1.61 (6 H, each s, isopropylidene Me), 3.63 (1 H, m, 5'-Ha), 3.98 (1 H, m, 5'-Hb), 4.43 (1 H, m, 4'-H), 4.79 (3 H, m, 1'-, 2'- and 3'-H), 6.58 (1 H, s, 3-H), 7.24 (1 H, d, J=8.7 Hz, 6-H), 7.97 (1 H, d, J=2.4 Hz, 9-H), 8.08 (1 H, dd, J=2.4 and 8.7 Hz, 7-H), 9.65, 13.05 (2 H, each br s, NH exchanges with D_2O). Hrms Found: m/z 405.1193. Calcd for $C_{18}H_{19}N_3O_8$; M^+, 405.1171.

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