Synthesis of 1,4-Diazepine Nucleosides

M. ZIA-UL-HAQ, Shahid HAMEED
Department of Chemistry, Quaid-I-Azam University, Islamabad-PAKISTAN
Helmut DUDDECK
Institute for Organic Chemistry, University of Hannover, Hannover-GERMANY
Roshan AHMED
Department of Chemistry, Quaid-I-Azam University, Islamabad-PAKISTAN
e-mail: roshan@hudson.isb.sdnPK.Org

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The phenolic $\beta$-diketones I prepared by modified Baker-Venkataraman rearrangement were converted to the flavones II in acidic medium which on treatment with aqueous ethylenediamine/propylenediamine gave diazepine derivatives III. After coupling with acetobromo sugars in the presence of mercuric cyanide and nitromethane, deacetylation in methanolic ammonia yielded nucleosides V. The structures of all the intermediates and final products were confirmed with the help of modern spectroscopic techniques.

Introduction

Several nucleosides such as 5-iodo-2-deoxyuridine, 1-$\beta$-D-arabinofuranosylcytosine and 1-$\beta$-D-ribofuranosyl-1,2,4-triazole-3-carboxamide (Ribovirin) have been used against herpes virus infections in man. For the clinical treatment of acquired immunodeficiency syndrome (AIDS), azidothymidine (AZT) and dideoxyinosine (DDI) have been approved, but they have a number of side effects. Therefore, during the last decade a number of new drugs have been synthesized and tested against the HIV-1 and HIV-2 viruses. Very few efforts have been directed towards the synthesis and testing of ring expanded nucleosides, the so-called “fat” nucleosides having seven membered diazepine ring systems.

The synthesis and biophysical characteristics of some ring expanded purine nucleosides have been reported. The synthesis of some [1,3]- and [1,4]-diazepine-5,8-dione nucleosides has also been reported. In all these nucleosides, the sugar moiety is attached to the five membered ring. There are only a few examples in which the sugar moiety is directly linked to seven membered rings.

Keeping in view the biological importance of nucleosides, it was planned to synthesize some novel 1,4-diazepine nucleosides by coupling with protected sugars. For this purpose, the phenolic $\beta$-diketones I synthesized in our laboratory by Baker-Venkataraman rearrangement were converted into flavones II, which on cyclocondensation with 1,2-diamines gave phenolic 1,4-diazepines III in good yield. The coupling of aza-heterocycles with acetobromosugars in the presence of Hg(CN)$_2$ in nitromethane, followed by deacetylation, afforded 1,4-diazepine nucleosides V (Scheme).
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**Scheme.** Synthesis of 1,4-diazepine nucleosides

Results and Discussion

Compounds **Ia** and **Ib** were prepared by two step-synthesis starting from \( \text{o-} \)hydroxy acetophenone and the corresponding benzoyl chloride by the well known Baker-Venkataraman rearrangement in 80-93% yield\(^{16}\). It was attempted to convert \( \beta \)-diketones **Ia** and **Ib** in acidic medium to get diazepine derivatives, but instead, the flavones **IIa** and **IIb**, respectively, were obtained. The formation of flavones was confirmed by their
The reactions of flavones \textbf{IIa} and \textbf{IIb} with aqueous ethylene diamine or propylene diamine solutions afforded 5-(2-hydroxyphenyl)-7-(4-substituted phenyl)-2,3-dihydro-1,4-diazepines \textbf{IIIa} to \textbf{IIIId} in fairly good yields. The IR spectra of these compounds exhibited C-H stretching vibrations due to a disubstituted benzene ring at 730 to 786 cm$^{-1}$ whereas N-H bending vibrations were observed at 1580 to 1582 cm$^{-1}$. The $^1$H-NMR spectra exhibited a singlet due to H-6 in the region of $\delta = 5.60$ to 5.85. The –CH$_2$- protons appeared as broad singlets in the region of $\delta = 3.35$ to 4.01. In the compounds \textbf{IIId} and \textbf{IIId}, a three proton doublet was present at $\delta = 1.4$ due to methyl protons at C-2. H-2 resonated at $\delta = 3.2$ in \textbf{IIId}, while in \textbf{IIId} it appeared at $\delta = 3.3$ as a multiplet. The N-H protons appeared as broad singlets at $\delta = 7.16$-7.55. In the mass spectra of the compounds \textbf{IIIa} to \textbf{IIId}, the molecular ion peak was also the base peak.

The phenolic 1,4-diazepine derivatives \textbf{IIIa} to \textbf{IIId} were coupled with 2,3,4,6-tetra-O-acetyl-D-glucopyranosyl bromide and 2,3,4,6-tetra-O-acetyl-D-galactopyranosyl bromide in the presence of mercuric cyanide and nitromethane. IR spectroscopic data exhibited carbonyl stretching of acetyl groups in the region 1709 to 1742 cm$^{-1}$. Free OH stretching vibrations were present at 3469 to 3511 cm$^{-1}$. In the $^1$H-NMR spectra of \textbf{IVa} to \textbf{IVd} the protons of acetyl groups appeared as singlets in the region $\delta = 1.84$ to 2.22. The anomeric protons in all these compounds resonated as broad singlets in the region $\delta = 5.28$ to 5.50. In compound \textbf{IVb} H=6 protons of glucopyranosyl resonated at $\delta = 4.28$ as a doublet of doublets with a geminal coupling constant of 12.5 Hz while in all other compounds these protons appeared as multiplets. In the $^{13}$C-NMR spectra of compounds \textbf{IVa} to \textbf{IVd} the methyl carbons of the acetyl groups resonated in the region $\delta = 20.5$ to 21.2 and the C = O of acetyl groups resonated at $\delta = 162.5$ to 170.8. The anomeric carbons in all these compounds resonated at $\delta = 91.9$ to 92.8, which indicated their linkage with a N-atom of the heterocyclic moiety. The molecular ion peaks with 100% intensity were observed for all these compounds in field-desorption mass spectra.

The deacetylation of compounds \textbf{IVa} to \textbf{IVd} was carried out successfully in methanolic ammonia in 51-64% yield. IR spectra of \textbf{Va} to \textbf{Vd} showed free OH bands in the region 3250 to 3500 cm$^{-1}$. The IR spectra of all these compounds lacked any signal due to carbonyl bands indicating complete deacetylation. In the $^1$H-NMR spectra doublets were observed due to anomeric protons which resonated in the region $\delta = 5.01$ to 5.06 with coupling constants of 7.2 to 7.7 Hz giving an indication of the axial orientation of this proton, hence showing the $\beta$-configuration of the monosaccharides.

Among the aromatic protons of a 4-substituted ring in \textbf{IVa} to \textbf{IVd}, H-2 and H-6 resonated in the region of $\delta = 7.72$ to 7.85 as doublets. These rather high values can be attributed to the fact that these protons are in the $\gamma$-position with respect to the imine nitrogen of heterocyclic moiety. This fact indicated the linkage of sugar moiety with nitrogen on the side of the phenolic ring. If the sugar moiety were linked with nitrogen present on the opposite side of the phenolic ring, a signal due to only one proton (H-6 of the phenolic ring) would have been observed in the high-frequency region which, however, is not the case in all these compounds. The deacetylation products \textbf{Va} to \textbf{Vd} also showed doublets due to H-2 and H-6 of a 4-substituted ring resonating in the region $\delta = 7.67$ to 7.77. The field-desorption mass spectra of all these compounds showed molecular ion peaks with 100% intensity. The purity of these compounds was confirmed by elemental analysis.
Experimental

The melting points were determined on a Gallenkamp digital melting point apparatus MFB-595-010M and are uncorrected. $^1$H and $^{13}$C NMR spectra were recorded on a Bruker DPX-400 instrument. Solvents used for NMR are given in the experimental part. All chemical shifts are referenced to TMS. The mass spectra were recorded on a Varian MAT CH-5 spectrometer.

General procedure for the synthesis of diazepines

A suspension of 0.01 moles of flavone IIa or IIb in 70% aqueous ethylene diamine or propylene diamine (30 ml) was refluxed for 2 – 3 h. The resulted orange red solution was cooled and diluted with ice cold water. The yellow solid obtained was filtered and recrystallized from benzene or ethanol.

5-(2-Hydroxyphenyl)-7-(4-chlorophenyl)-2,3-dihydro-1,4-diazepine (IIIa) m. p. = 241.0 – 242.3°C. Yield = 59.0%. IR ($\nu_{\text{max}}$, KBr, cm$^{-1}$): 3430, 2746, 1581, 1425, 1254, 1137, 987, 831. $^1$H-NMR (CDCl$_3$, $\delta$-values): 3.63 (bs, 2H, CH$_2$), 3.93 (bs, 2H, CH$_2$), 5.71 (s, 1H, =C-H), 7.25 (m, 6H, Ar-H), 7.33 (m, 2H, Ar-H), 7.55 (bs, 2H, NH & OH). Mass [m/z (% )]: 298 (M$^+$, 100), 297 (96), 281 (19), 270 (16), 187 (11), 178 (34), 160 (12).

5-(2-Hydroxyphenyl)-7-(4-methoxyphenyl)-2,3-dihydro-1,4-diazepine (IIIb) m. p. = 220–228°C. Yield = 62.0%. IR ($\nu_{\text{max}}$, KBr, cm$^{-1}$): 3382, 2830, 1580, 1464, 1251, 1143, 984, 831, 786, 750. $^1$H-NMR (CDCl$_3$, $\delta$-values): 3.71 (bs, 2H, CH$_2$), 3.87 (s, 3H, OCH$_3$), 3.93 (bs, 2H, CH$_2$), 5.82 (s, 1H, =C-H), 6.90 (m, 2H, Ar-H), 7.30 (m, 4H, Ar-H), 7.60 (m, 2H, Ar-H), 7.70 (bs, 2H, NH & OH). Mass [m/z (% )]: 294 (M$^+$, 100), 208 (1), 201 (1), 174 (31), 160 (15), 147 (15), 104 (4), 91 (4).

2-Methyl-5-(2-hydroxyphenyl)-7-(4-chlorophenyl)-2,3-dihydro-1,4-diazepine (IIIc) m. p. = 217 – 218°C. Yield = 39.0%. IR ($\nu_{\text{max}}$, KBr, cm$^{-1}$): 3460, 2880, 1582, 1434, 1254, 932. $^1$H-NMR (CDCl$_3$, $\delta$-values): 1.40 (d, 3H, CH$_3$), 3.20 (m, 1H, CH), 3.35 (m, 2H, CH$_2$), 5.60 (s, 1H, =C-H), 7.50-7.80 (m, 8H, Ar-H), 8.18 & 8.27 (2 x bs, NH & OH). Mass [m/z (% )]: 312 (M$^+$, 100), 311 (98), 295 (28), 284 (19), 270 (44), 269 (22), 192 (23), 174 (9).

2-Methyl-5-(2-hydroxyphenyl)-7-(4-methoxyphenyl)-2,3-dihydro-1,4-diazepine (IIId) m. p. = 198.0 – 198.5°C. Yield = 53.0%. IR ($\nu_{\text{max}}$, KBr, cm$^{-1}$): 3442, 2844, 1580, 1438, 1238, 730. $^1$H-NMR (CDCl$_3$, $\delta$-values): 1.40 (d, 3H, CH$_3$), 3.30 (m, 1H, CH), 3.60 (m, 2H, CH$_2$), 3.78 (s, 3H, OCH$_3$), 5.70 (s, 1H, =C-H), 6.70-6.85 (m, 2H, Ar-H), 7.15-7.23 (m, 4H, Ar-H), 7.40 (m, 2H, Ar-H), 7.60 (bs, 2H, NH & OH). Mass [m/z (% )]: 308 (M$^+$, 100), 307 (90), 291 (24), 266 (44), 237 (11), 188 (38), 174 (15), 132 (18).

General procedure for the synthesis of N-glycosides

To a mixture of 2.0 mmoles of acetobromosugar (2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide or 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide), 2.0 mmoles of mercuric cyanide and 2.0 g of anhydrous calcium sulphate in 30 ml of dry nitromethane was added 1 mmole of the 1,4-diazepine (III). The mixture was refluxed for 2-4 h, filtered while still hot, washed with more hot nitromethane and the filtrate evaporated to dryness in vacuo. The product obtained was treated with dichloromethane and filtered to separate the solid (a complex formed by mercuric halide and the corresponding heterocycles). The dichloromethane extract was washed with 30% aqueous potassium iodide and water and dried over anhydrous sodium sulphate. The solvent, after filtration, was evaporated in vacuo and purification was carried out using...
column chromatography.

N-4-(2,3,4,6-tetra-O-Acetyl-β-D-galactopyranosyl)-5-(2-hydroxyphenyl)-7-(4-chlorophenyl)-2,3-dihydro-1,4-diazepine (IVa) m. p. = 113 – 115°C. Yield = 38.0%. 1H-NMR (CDCl₃, δ-values): 1.03 (d, 3H, CH₃), 1.84 (s, 3H, CH₃CO), 1.86 (s, 3H, CH₃CO), 1.91 (s, 3H, CH₃CO), 1.96 (s, 3H, CH₃CO), 3.99-4.24 (m, 3H, H-2/3), 4.90-4.92 (m, 3H, 4.99-5.11 (m, 2H), 5.28 (m, 2H), 6.99-7.11 (m, 2H, Ar-H), 7.23 (m, 2H, Ar-H), 7.44-7.56 (m, 3H, Ar-H and H-6), 7.79-7.85 (m, 2H, Ar-H), 9.36 (bs, 1H, OH). 13C-NMR (CDCl₃, δ-values): 54.93 (C-2), 60.08 (C-3), 99.03 (C-6), 153.36 (C-7), 161.35 (C-5). [sugar carbons: 20.46 (CH₃), 20.77 (CH₃), 20.85 (CH₃), 21.22 (CH₃), 61.09 (C-6), 67.23 (C-5), 68.29 (C-2), 71.73 (C-4), 71.84 (C-3), 92.55 (C-1), 169.76 (CO), 169.78 (CO), 169.99 (CO), 170.44 (CO), [4-substituted phenyl carbons: 114.09 (C-3/5), 130.33 (C-2/6), 132.42 (C-1), 139.77 (C-4)], phenolic ring carbons: 115.87 (C-3), 124.10 (C-5), 124.79 (C-1), 130.93 (C-6), 133.36 (C-4), 165.51 (C-2)]. Mass FD m/z (rel. int.) M⁺ = 625 (100%).

N-4-(2,3,4,6-tetra-O-Acetyl-β-D-glucopyranosyl)-2-methyl-5-(2-hydroxyphenyl)-7-(4-methoxyphenyl)-2,3-dihydro-1,4-diazepine (IVb) m. p. = 97.6 – 98.0°C. Yield = 35.0%. 1H-NMR (CDCl₃, δ-values): 1.90 (s, 3H, CH₃CO), 1.95 (s, 6H, 2 x CH₃CO), 1.98 (s, 3H, CH₃CO), 3.80 (s, 3H, OCH₃), 3.87 (t, 2H, H-3), 4.05 (t, 2H, H-2), 7.20 (s, 1H, H-6), 8.12 (s, 1H, OH) [sugar protons: 4.28 (m, 2H, H-6A, J₆₋₆B = 6.5 Hz, J₆₋₆B = 6.5 Hz), 5.05 (t, 1H, H-3, J₃₋₄ = 11.8 Hz, 5.1-5.3 (m, 4H, H-2,4,5,6), 5.38 (bs, 1H, H-1)], [4-substituted phenyl protons: 7.62 (d, 2H, H-3, J₃₋₄ = 8.0 Hz, 9.8 Hz), 7.75 (d, 2H, H-6, J₆₋₆B = 8.5 Hz), 7.15 (t, 1H, H-5), 7.15 (t, 1H, H-4, J₄₋₅ = 8.2 Hz), 7.50 (d, 1H, H-6, J₆₋₆B = 7.7 Hz)]. 13C-NMR (CDCl₃, δ-values): 48.32 (C-3), 49.84 (C-2), 98.87 (C-6), 126.88 (C-7), 129.09 (C-5), [sugar carbons: 20.53 (CH₃), 20.57 (CH₃), 20.73 (CH₃), 20.86 (CH₃), 60.96 (C-6), 68.14 (C-2), 70.98 (C-4), 72.52 (C-3), 72.53 (C-5), 91.93 (C-1), 162.48 (CO), 165.93 (CO), 169.30 (CO), 169.38 (CO), [4-substituted phenyl carbons: 116.44 (C-3/5), 130.13 (C-1), 130.77 (C-2/6), 137.58 (C-4)], phenolic ring carbons: 115.87 (C-3), 123.97 (C-5), 126.49 (C-1), 130.61 (C-6), 132.64 (C-4), 163.24 (C-2)]. Mass FD m/z (rel. int.) M⁺ = 625 (100%).

N-4-(2,3,4,6-tetra-O-Acetyl-β-D-glucopyranosyl)-2-methyl-5-(2-hydroxyphenyl)-7-(4-chlorophenyl)-2,3-dihydro-1,4-diazepine (IVc) m. p. = 104.4 – 105.0°C. Yield = 29.5%. 1H-NMR (CDCl₃, δ-values): 1.35 (d, 3H, CH₃), 3.97-4.18 (m, 3H, H-2/3), 7.28 (s, 1H, H-6), 8.18 (bs, 1H, OH) [sugar protons: 1.96 (s, 3H, CH₃CO), 2.04 (s, 6H, 2 x CH₃CO), 2.22 (s, 3H, CH₃CO), 3.87 (s, 3H, OCH₃), 4.27-4.43

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N-Methyl-3,4,5,6-tetrahydro-1,4-diazepine (m, 2H, H-6), 5.19 (dd, 1H, H-3), 3.50-5.55 (m, 3H, H-2/4/5), 5.50 (bs, 1H, H-1)], [4-substituted phenyl protons: 7.02 (d, 2H, H-3/5), 7.78 (d, 2H, H-2/6)], [phenolic ring protons: 7.18-7.27 (m, 2H), 7.53-7.62 (m, 2H)]. \(^{13}C\)-NMR (CDCl\(_3\), \(\delta\)-values): 55.84 (C-2), 61.02 (C-3), 99.15 (C-6), 153.18 (C-7), 161.70 (C-5), [sugar carbons: 20.49 (CH\(_3\)), 20.72 (CH\(_3\)), 20.76 (CH\(_3\)), 20.88 (CH\(_3\)), 61.12 (C-6), 66.91 (C-5), 68.65 (C-2), 70.48 (C-3), 72.20 (C-4), 92.67 (C-1), 169.76 (CO), 169.89 (CO), 170.32 (CO), 170.79 (CO)], [4-substituted phenyl carbons: 115.01 (C-3/5), 131.79 (C-2/6), 133.41 (C-1), 139.92 (C-4)], [phenolic ring carbons: 115.08 (C-3), 123.99 (C-5), 126.30 (C-1), 130.52 (C-6), 133.40 (C-4), 165.09 (C-2)]. Mass FD m/z (rel. int.) \(M^+ = 639\) (100%).

**General procedure for deacetylation**

One mmole of the acetylated nucleoside was dissolved in 100 ml of dry methanol and a fairly rapid stream of dry ammonia was passed into the solution for 2 h. The solution was kept at 0-5°C for 20 h, filtered and then concentrated to a syrup under reduced pressure at room temperature. Methanol was added again to dissolve the syrup and again evaporated to a small volume. Purification was carried out by column chromatography using silica gel as adsorbent.

**N-4-(\(\beta\)-D-Galactopyranosyl)-5-(2-hydroxyphenyl)-7-(4-chlorophenyl)-2,3-dihydro-1,4-diazepine** (Va) m. p. = 173.0°C. Yield = 64.0%. UV \(\{\lambda_{max}(\epsilon)\text{nm}\}\): 356.0 (20798.6), 266.6 (21085.1), 228.3 (23997). IR \(\nu_{max}\) (KBr, cm\(^{-1}\)):

- 3250, 3075, 2900, 1581, 1504, 1484, 1220, 1050, 742.
- \(^1\)H-NMR (CD\(_3\)OD, \(\delta\)-values): 4.54 (bs, 4H, H-2/3), 7.16-7.20 (m, 3H, Ar-H and H-6), 7.40-7.42 (d, 1H, J = 7.9 Hz, Ar-H), 7.50-7.55 (m, 3H, Ar-H), 7.69-7.72 (d, 2H, Ar-H), [sugar protons: 3.15 (m, 1H, H-2), 3.31 (m, 2H, H-4/5), 3.45 (m, 1H, H-3), 3.59 (dd, H-6A, \(J_{gA,6A} = 9.7\) Hz, \(J_{gA,5} = 3.3\) Hz), 3.90 (dd, H-6B, \(J_{gB,6A} = 9.7\) Hz, \(J_{gB,5} = 3.3\) Hz), 5.01 (d, 1H, J = 7.7 Hz, H-1), 5.50 (s, 4H, OH)]. Mass FD m/z (rel. int.) \(M^+ = 461\) (100%).

**C\(_{23}\)H\(_{25}\)O\(_3\)N\(_2\)Cl:** calcd. C 59.93, H 5.46, N 6.07, Found C 60.10, H 5.36, N 6.10.

**N-4-(\(\beta\)-D-Glucopyranosyl)-5-(2-hydroxyphenyl)-7-(4-methoxyphenyl)-2,3-dihydro-1,4-diazepine** (Vb) m. p. = 151.5 - 153.0°C. Yield = 63.0%. UV \(\{\lambda_{max}(\epsilon)\text{nm}\}\): 356.0 (27910.8), 260.8 (26489.9), 224.6 (31619.0). IR \(\nu_{max}\) (KBr, cm\(^{-1}\)):

- 3250, 3052, 2891, 1590, 1560, 1511, 1344, 1238, 1037, 760.
- \(^1\)H-NMR (CD\(_3\)OD, \(\delta\)-values): 3.58 (s, 3H, OCH\(_3\)), 4.54 (bs, 4H, H-2/3), 7.19 (t, 1H, Ar-H), 7.40 (d, 1H, J = 8.4 Hz, Ar-H), 7.50-7.54 (m, 4H, Ar-H and H-6), 7.56-7.60 (m, 1H, Ar-H), 7.69-7.71 (d, 2H, Ar-H), [sugar protons: 3.15 (m, 1H, H-2), 3.32 (m, 2H, H-4/5), 3.43 (m, 1H, H-3), 3.68 (dd, H-6A, \(J_{gA,6A} = 12.0\) Hz, \(J_{gA,5} = 5.4\) Hz), 3.85 (dd, H-6B, \(J_{gB,6A} = 12.0\) Hz, \(J_{gB,5} = 2.3\) Hz), 5.04 (d, 1H, J = 7.7 Hz, H-1), 5.50 (s, 4H, OH)].

**C\(_{24}\)H\(_{28}\)O\(_3\)N\(_2\)Cl:** calcd. C 63.14, H 5.18, N 6.13, Found C 63.35, H 6.10, N 6.20.

**N-4-(\(\beta\)-D-Glucopyranosyl)-2-methyl-5-(2-hydroxyphenyl)-7-(4-chlorophenyl)-2,3-dihydro-1,4-diazepine** (Ve) m. p. = 162 - 163°C. Yield = 55.0%. UV \(\{\lambda_{max}(\epsilon)\text{nm}\}\): 356.0 (21777.9), 262.8 (20686.6), 224.1 (24523.7). IR \(\nu_{max}\) (KBr, cm\(^{-1}\)):

- 3450, 3390, 1670, 1590, 1370, 1320, 1180, 1110, 550.
- \(^1\)H-NMR (CD\(_3\)OD, \(\delta\)-values): 1.92 (d, 3H, CH\(_3\)), 4.54 (bs, 3H, H-2/3), 7.17-7.21 (m, 2H, Ar-H), 7.40 (d, 1H, J = 7.3 Hz, Ar-H), 7.50-7.55 (m, 4H, Ar-H and H-6), 7.67-7.71 (d, 2H, Ar-H), [sugar protons: 3.15 (m, 1H, H-2), 3.31 (m, 2H, H-4/5), 3.43 (m, 1H, H-3), 3.66 (m, 1H, H-6A), 3.85 (m, 1H, H-6B), 5.06 (d, 1H, J = 7.5 Hz, H-1), 5.47 (s, 4H, OH)]. Mass FD m/z (rel. int.) \(M^+ = 475\) (100%).

**C\(_{24}\)H\(_{27}\)O\(_6\)N\(_2\)Cl:** calcd. C 60.69, H 5.73, N 5.89, Found C 60.75, H 5.72, N 5.95.

**N-4-(\(\beta\)-D-Galactopyranosyl)-2-methyl-5-(2-hydroxyphenyl)-7-(4-methoxyphenyl)-2,3-
dihydro-1,4-diazepine (Vd) m. p. = 133.0-135.0°C. Yield = 51.0%. UV \( \lambda_{max}(nm) \): 356.2 (29948.4), 261.0 (17886.8), 226.5 (29945.7). IR (\( \nu_{max} \), KBr, cm\(^{-1} \)): 3500, 3210, 2900, 2801, 1690, 1110, 771, 660.

\(^1\)H-NMR (CD\(_3\)OD, \( \delta \)-values): 1.92 (d, 3H, CH\(_3\)), 3.73 (s, 3H, OCH\(_3\)), 4.55 (bs, 3H, H-2/3), 7.03-7.08 (m, 2H, Ar-H), 7.16-7.19 (m, 1H, Ar-H), 7.39 (d, 1H, J = 7.8 Hz, Ar-H), 7.46-7.53 (m, 3H, Ar-H and H-6), 7.65-7.69 (m, 2H, Ar-H), [sugar protons: 3.15 (m, 1H, H-2), 3.31 (m, 2H, H-4/5), 3.42 (m, 1H, H-3), 3.69 (dd, 1H, \( \delta_{6A,B} = 6.1 \) Hz, \( \delta_{6A,5} = 1.1 \) Hz), 3.90 (d, 1H, H-6B, J = 3.5 Hz), 5.03 (d, 1H, J = 7.5 Hz, H-1), 5.50 (s, 4H, OH)]. Mass FD m/z (rel. int.) \( M^+ = 471 \) (100%). C\(_{25}\)H\(_{30}\)O\(_7\)N\(_2\): calcd. C 63.81, H 6.42, N 5.95, Found C 63.40, H 6.40, N 6.01.

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References

15. P.A. Sutton, V. Cody and E. Marquez, Nucleosides and Nucleotides, 6(3), 613 (1987).