Chemistry of 1,3-Dioxepins. XI.\textsuperscript{1} 
Bis-(4,7-dihydro-1,3-dioxepin) Approach to Pyridoxine Intermediates 1,5-Dihydro-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridin-9-ols\textsuperscript{†}

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Received April 17, 1996; revised September 5, 1996; accepted September 7, 1996

The novel pyridoxine intermediates, bis-dioxepino[5,6-c]pyridin-9-ols 3 and 4 have been synthesized starting from bis-(4,7-dihydro-1,3-dioxepins) 1. Their constitution and configuration has been confirmed by single-crystal X-ray diffractions of bis-dioxepins 1a and 1b, dioxepinopyridinol 3a maleate salt, as well as 3b and 4b monohydrates.

INTRODUCTION

Syntheses of 1,5-dihydro-8-methyl-3H-[1,3]dioxepino-[5,6-c]pyridin-9-ols, pyridoxine (vitamin B\textsubscript{6}) intermediates, starting from the different kinds of 4,7-dihydro-1,3-dioxepins are of our current interest.\textsuperscript{2–7} Related to the above, we studied the syntheses and/or application of 5-substituted-4,7-dihydro-1,3-dioxepins.\textsuperscript{8–12} Now, we would like to report a bis-(4,7-dihydro-1,3-dioxepin) approach to the novel pyridoxine intermediates, 1,5-dihydro-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridin-9-ols 3 and 4 (Scheme 1).

\textsuperscript{†} Dedicated to the memory of the late Professor Stanko Borčić.

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Scheme 1.
RESULTS AND DISCUSSION

Despite of the simplicity of their structure, the starting bis-(4,7-dihydro-1,3-dioxepins) 1 have not been hitherto studied in any great detail. The only products synthesized so far, 1b–d, are covered by patents and their preparative methods and physical constants are not well known.\textsuperscript{13–15} Therefore, we prepared 1 by the known acetalization/transacetalization procedures\textsuperscript{16} of cis-2-butene-1,4-diol with glutardialdehyde, terephtalaldehyde and 1,1,3,3-tetra-methoxypropane, respectively. Otherwise, we prepared the hitherto unknown bis-dioxepin 1a, accompanied by viscous oligomeric material,\textsuperscript{17} in 55.6%, (m.p. 101–102 °C from acetone) according to the Sprung and Guenther procedure,\textsuperscript{18} i.e. by p-toluenesulfonic acid catalyzed reaction of cis-2-butene-1,4-diol with glyoxal (mol ratio 2.4 to 1) in toluene, under azeotropic removal of reaction formed water.

Physical data of the thus obtained bis-dioxepins 1 were consistent with literature data,\textsuperscript{13–15} and \textsuperscript{1}H- and \textsuperscript{13}C-NMR data (Table I) with the prepositional structures. However, the configurations of 1a and 1b were confirmed by X-ray diffraction (Figure 1, Table II).\textsuperscript{19}

![Figure 1. PLUTON plots of some bis-dioxepins 1 and dioxepinopyridinols 3 and 4.](image-url)
**TABLE I**

$^1$H- and $^{13}$C-NMR data of bis-(1,3-dioxepin) derivate 1, 3, 4 and 7

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>$^1$H-NMR, 300 MHz, δ/ppm (DMSO-d$_6$, 25 °C, TMS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>5.68 (t, 4H, $J_{1,8}$, H-C5, 6&amp;5',6'); 4.65 (s, 2H, H-C2&amp;2'); 4.52–4.02 (m, 8H, H-C4, 7&amp;4',7)</td>
</tr>
<tr>
<td>1b</td>
<td>5.81 (s, 4H, H-C5, 6&amp;5',6'); 4.91 (t, 2H, $J_{2,5}$, H-C2&amp;2'); 4.34 &amp; 4.22 (dd, 8H, $J_{14,9}$, H-C4, 7&amp;4',7); 2.02 (t, 2H, $J_{5,8}$, -CH$_2$-)</td>
</tr>
<tr>
<td>1c</td>
<td>5.61 (s, 4H, H-C5, 6&amp;5',6'); 4.63 (t, 2H, $J_{5,6}$, H-C2&amp;2'); 4.21 &amp; 4.00 (dd, 8H, $J_{15,4}$, H-C4, 7&amp;4',7); 1.53–1.46 (m, 4H, -CH$_2$-CH$_2$-CH$_2$-); 1.32–1.24 (m, 2H, -CH$_2$-CH$_2$-CH$_2$-)</td>
</tr>
<tr>
<td>1d*</td>
<td>7.54 (s, 4H, H-arom.); 5.86 (s, 2H, H-C2&amp;2'); 5.80 (s, 4H, H-C5, 6&amp;5',6'); 4.39 &amp; 4.28 (dd, 8H, $J_{14,9}$, H-C4, 7&amp;4',7)</td>
</tr>
<tr>
<td>3a**</td>
<td>8.88 (br, 1H, OH); 7.81 (s, 1H, H-C6); 5.70 (s, 2H, H-C5,6'); 5.25–4.71 (m, 6H, H-C1,3,5&amp;2'); 4.44 &amp; 4.15 (dd, 4H, $J_{15,1}$, H-C4',7'); 2.36 (s, 3H, H-C10)</td>
</tr>
<tr>
<td>3a**</td>
<td>7.50–6.30 (br, 3H, OH &amp; COOH); 7.94 (s, 1H, H-C6); 6.18 (s, 2H, -CH$<em>2$-); 5.70 (s, 2H, H-C5,6'); 5.37–4.68 (m, 6H, H-C1,3,5&amp;2'); 4.44 &amp; 4.15 (dd, 4H, $J</em>{14,7}$, H-C4',7'); 2.42 (s, 3H, H-C10)</td>
</tr>
<tr>
<td>3b</td>
<td>8.98 (br, 1H, OH); 7.82 (s, 1H, H-C6); 5.71 (s, 2H, H-C5,6'); 5.19–4.70 (m, 6H, H-C1,3,5&amp;2'); 4.33 &amp; 4.12 (dd, 4H, $J_{15,2}$, H-C4',7'); 2.37 (s, 3H, H-C10); 1.93 (t, 2H, $J_{5,6}$, -CH$_2$-)</td>
</tr>
<tr>
<td>3c</td>
<td>8.96 (br, 1H, OH); 7.81 (s, 1H, H-C6); 5.70 (s, 2H, H-C5,6'); 5.17–4.67 (m, 6H, H-C1,3,5&amp;2'); 4.29 &amp; 4.09 (dd, 4H, $J_{14,7}$, H-C4',7'); 2.37 (s, 3H, H-C10); 1.62–1.55 (m, 4H, -CH$_2$-CH$_2$-CH$_2$-); 1.55–1.35 (m, 2H, -CH$_2$-CH$_2$-CH$_2$-)</td>
</tr>
<tr>
<td>3d</td>
<td>9.00 (br, 1H, OH); 7.85 (s, 1H, H-C6); 7.48 (s, 4H, H-arom.); 6.00 &amp; 5.83 (2 s, 2H, H-C3 &amp; 2'); 5.76 (s, 2H, H-C5,6'); 5.11 &amp; 4.88 (dd, 2H, $J_{15,4}$, H-C1); 4.91 &amp; 4.86 (dd, 2H, $J_{14,2}$, H-C5); 4.29 &amp; 4.25 (dd, 4H, $J_{13,7}$, H-C4',7'); 2.38 (s, 3H, H-C10)</td>
</tr>
<tr>
<td>4a</td>
<td>8.85 (br, 2H, OH); 7.82 (s, 2H, H-C6&amp;6'); 5.31–4.75 (m, 10H, H-C1,3,5 &amp; 1,3',5'); 2.39 (s, 6H, H-C10 &amp;10')</td>
</tr>
<tr>
<td>4b</td>
<td>8.99 (br, 2H, OH); 7.83 (s, 2H, H-C6&amp;6'); 5.17 &amp; 4.76; (dd, 4H, $J_{15,3}$, H-C1, 1'); 5.06 (t, 2H, $J_{5,0}$, H-C3 &amp;3'); 4.85 &amp; 4.79 (dd, 4H, $J_{13,4}$, H-C5 &amp; 5'); 2.37 (s, 6H, H-C10 &amp;10'); 1.99 (t, 2H, $J_{5,0}$, -CH$_2$-)</td>
</tr>
<tr>
<td>4c</td>
<td>8.90 (br, 2H, OH); 7.82 (s, 2H, H-C6&amp;6'); 5.18–4.67 (m, 10H, H-C1,3,5 &amp; 1,3',5'); 2.37 (s, 6H, H-C10 &amp;10'); 1.67–1.56 (m, 4H, -CH$_2$-CH$_2$-CH$_2$-); 1.55–1.43 (m, 2H, -CH$_2$-CH$_2$-CH$_2$-)</td>
</tr>
<tr>
<td>7a</td>
<td>8.26 (s, 2H, H-C6&amp;6'); 5.11–4.74 (m, 10H, H-C1,3,5 &amp; 1,3',5'); 2.41 (s, 6H, COCH$_3$); 2.31 (s, 6H, H-C10 &amp;10')</td>
</tr>
<tr>
<td>7b</td>
<td>8.31 (s, 2H, H-C6&amp;6'); 8.22–7.63 (m, 10H, H-arom.); 5.16–4.79 (m, 10H, H-C1,3,5 &amp; 1,3',5'); 2.33 (s, 6H, H-C10 &amp;10')</td>
</tr>
<tr>
<td>7c</td>
<td>10.58 (s, 2H, NH); 8.31 (s, 2H, H-C6&amp;6'); 7.91 (s, 8H, H-arom.); 5.09–4.70 (m, 10H, H-C1,3,5 &amp; 1,3',5'); 2.15 (s, 6H, H-C10 &amp;10'); 2.10 (s, 6H, COCH$_3$)</td>
</tr>
</tbody>
</table>

* Spectra were taken in CDCl$_3$
** 3a maleate salt
Table I – (continued)

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>$^{13}$C-NMR, 75 MHz, $\delta$/ppm (DMSO-$d_6$, 25 °C, TMS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>129.12 (C5,6&amp;5',6'); 101.24 (C2&amp;2'); 65.46 (C4,7&amp;4',7')</td>
</tr>
<tr>
<td>1b</td>
<td>129.71 (C5,6&amp;5',6'); 100.98 (C2&amp;2'); 64.77 (C4,7&amp;4',7'); 37.57 (-CH$_2$-)</td>
</tr>
<tr>
<td>1c</td>
<td>129.82 (C5,6&amp;5',6'); 103.63 (C2&amp;2'); 64.56 (C4,7&amp;4',7'); 32.95 (-CH$_2$-CH$_2$-); 19.96 (-CH$_2$-CH$_2$-CH$_2$-)</td>
</tr>
<tr>
<td>1d*</td>
<td>138.88 &amp; 126.16 (C-arom.); 129.77 (C5,6&amp;5',6'); 101.84 (C2&amp;2'); 64.44 (C4,7&amp;4',7')</td>
</tr>
<tr>
<td>3a</td>
<td>147.29, 146.51, 138.09, 133.64 &amp; 133.24 (C5a,6,8,9&amp;9a); 129.57 (C5',6'); 103.50 (C3); 101.96 (C2'); 66.48, 65.69 &amp; 64.28 (C1&amp;4',7&amp;5); 19.75 (C10)</td>
</tr>
<tr>
<td>3a**</td>
<td>167.10 (COOH) ; 148.59, 144.70, 137.70, 134.88 &amp; 132.56 (C5a,6,8,9,9a&amp;-CH$_2$-); 129.57 (C5',6'); 103.10 (C3); 100.91 (C2'); 65.66 &amp; 64.34 (C1,5&amp;4',7'); 18.06 (C10)</td>
</tr>
<tr>
<td>3b</td>
<td>147.60, 146.90, 138.33, 134.14 &amp; 133.79 (C5a,6,8,9&amp;9a); 129.97 (C5',6'); 104.17 (C3); 100.82 (C2'); 66.69, 64.82 &amp; 63.69 (C1&amp;4',7&amp;5); 38.07 (-CH$_2$-); 19.81 (C10)</td>
</tr>
<tr>
<td>3c</td>
<td>147.49, 146.80, 138.31, 134.24 &amp; 133.89 (C5a,6,8,9&amp;9a); 130.05 (C5',6'); 106.73 (C3); 103.75 (C2'); 66.54, 64.68 &amp; 63.45 (C1&amp;4',7&amp;5); 33.36 &amp; 32.93 (-CH$_2$-CH$_2$-CH$_2$-); 19.74 (C10); 19.71 (-CH$_2$-CH$_2$-CH$_2$-)</td>
</tr>
<tr>
<td>3d</td>
<td>147.42, 146.52, 139.41, 133.78 &amp; 133.33 (C5a,6,8,9&amp;9a); 138.75, 138.15, 126.28 &amp; 126.18 (C-arom.); 129.92 (C5',6'); 103.89 (C3); 101.41 (C2'); 66.09, 64.47 &amp; 63.15 (C1&amp;4',7&amp;5); 19.72 (C10)</td>
</tr>
<tr>
<td>4a</td>
<td>147.32, 146.61, 138.05, 133.75 &amp; 133.09 (C5a,6,8,9,9a&amp;5a',6',8',9',9a'); 103.31 (C3&amp;3'); 66.39 (C1&amp;1'); 64.30 (C5&amp;5'); 19.25 (C10&amp;10')</td>
</tr>
<tr>
<td>4b</td>
<td>147.33, 146.64, 138.15, 133.90 &amp; 133.52 (C5a,6,8,9,9a&amp;5a',6',8',9',9a'); 103.61 (C3&amp;3'); 66.53 (C1&amp;1'); 63.58 (C5&amp;5'); 38.54 (-CH$_2$-); 19.79 (C10&amp;10')</td>
</tr>
<tr>
<td>4c</td>
<td>147.58, 146.84, 138.31, 134.31 &amp; 133.96 (C5a,6,8,9,9a&amp;5a',6',8',9',9a'); 106.79 (C3&amp;3'); 66.60 (C1&amp;1'); 63.51 (C5&amp;5'); 33.39 (-CH$_2$-CH$_2$-CH$_2$-); 19.78 (C10&amp;10'); 19.54 (CH$_2$-CH$_2$-CH$_2$)</td>
</tr>
<tr>
<td>7a</td>
<td>–</td>
</tr>
<tr>
<td>7b</td>
<td>163.93 (CO); 152.42, 144.68, 141.99, 139.90, 134.94, 133.83, 130.16, 129.28 &amp; 127.66 (C5a,6,8,9,9a&amp;5a',6',8',9',9a&amp;C-arom.); 102.83 (C3&amp;3'); 66.35 (C1&amp;1'); 63.80 (C5&amp;5'); 19.09 (C10&amp;10')</td>
</tr>
<tr>
<td>7c</td>
<td>169.85 (CO); 152.07, 145.81, 145.71, 142.01, 141.04, 134.39, 129.98, 127.67 &amp; 119.31 (C5a,6,8,9,9a&amp;5a',6',8',9',9a&amp;C-arom.); 103.14 (C3&amp;3'); 66.71 (C1&amp;1'); 63.92 (C5&amp;5'); 24.31 (COCH$_3$); 19.59 (C10&amp;10')</td>
</tr>
</tbody>
</table>

* Spectra were taken in CDCls
** 3a maleate salt

In our experiment, all of the thus synthesized bis-dioxepins 1 underwent the Diels-Alder cycloaddition with 4-methylloxazole$^{20}$ or its 5-ethoxy-$^{21}$ and 5-cyano-$^{22}$ derivatives 2a–c at 130–190 °C, furnishing the mixture of bis-di-
Table II
Summary of some essential crystallographic data for bis-dioxepin derivates:

<table>
<thead>
<tr>
<th></th>
<th>1a</th>
<th>1b</th>
<th>3a maleate salt</th>
<th>3b x H₂O</th>
<th>4b x H₂O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystal system</td>
<td>triclinic</td>
<td>triclinic</td>
<td>monoclinic</td>
<td>monoclinic</td>
<td>monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P 1</td>
<td>P 1</td>
<td>P 2₁/n</td>
<td>P 2₁/c</td>
<td>P 2₁/n</td>
</tr>
<tr>
<td>a/Å</td>
<td>4.348 (2)</td>
<td>6.367 (4)</td>
<td>6.465 (3)</td>
<td>13.096 (3)</td>
<td>6.550 (1)</td>
</tr>
<tr>
<td>b/Å</td>
<td>6.014 (2)</td>
<td>9.113 (8)</td>
<td>20.720 (7)</td>
<td>10.050 (3)</td>
<td>8.987 (2)</td>
</tr>
<tr>
<td>α/deg</td>
<td>91.50 (4)</td>
<td>67.50 (2)</td>
<td>90</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>β/deg</td>
<td>93.64 (3)</td>
<td>73.47 (3)</td>
<td>95.61 (2)</td>
<td>108.27 (2)</td>
<td>98.55 (2)</td>
</tr>
<tr>
<td>γ/deg</td>
<td>103.74 (3)</td>
<td>73.54 (5)</td>
<td>90</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>Reference</td>
<td>19</td>
<td>24</td>
<td>23</td>
<td>24</td>
<td>24</td>
</tr>
</tbody>
</table>

a X-ray diffractions were performed on a Phillips PW1100 diffractometer with Mo-Kα radiation and graphite monochromator. For further details of crystal structure determinations see the above References.

Oxepinopiridinols 3 and 4. Thus, refluxing of 1a in a twelve molar excess of 5-cyano-4-methyloxazole (2c) in the presence of 2,6-di-tert-butyl-4-methylphenol as antioxidant and p-toluenesulfonic acid as catalyst for 15 hours produced a mixture of products, accompanied by a solid polymeric material which, after separation and purification by column chromatography gave dioxepino[5,6-c]pyridin-9-ols 3a (20.1%) and 4a (4.4%), respectively.

In an analogous manner, using other bis-dioxepins 1 and oxazoles 2, dioxepino[5,6-c]pyridin-9-ols 3b–d and 4b–c were obtained in low to moderate yields (Scheme 1).

We suggest that formation of 4 is the consequence of a consecutive reaction, confirmation of which is done by the parallel preparation of 4 from 3 under the above cited reaction conditions.

In the case of acetic anhydride catalyzed cycloadditions, small quantities of one or two additional, hitherto to us unknown pyridinol derivatives were detected by TLC (red spots by Pauly- and blue by Gibbs reagents), unfortunately, not isolated and characterized so far. Because of their increased presence in the case of [4 + 2]-cycloaddition of 2 to 3, and the well known reactivity of pyridinol derivatives with acetic anhydride, we supposed that they could be the mono-O-acetyl derivatives of 4 and/or the possible nonaromatic cycloadduct-precursor to 4.
The structures of 3 and 4 were assigned from analytical, NMR- (Table I) and MS (Figure 2) spectral data as well as by the parallel three steps synthesis of the 3a following sequences: 1a→5→6→3a in an overall yield of 14.4%.[11]

Additionally, the configuration of 3 was confirmed by the single crystal X-ray diffractions of 3a maleate salt[23] and of 3b monohydrate (m.p. 112–114 °C), obtained by crystallization of 3b from wet ethyl acetate (Figure 1).

Despite several attempts, it was not possible to prepare a sample of 4a of acceptable elemental analysis. Therefore, we turned our attention to the preparation of a good-quality single crystal suitable for X-ray structure analysis. Unfortunately, neither the single crystal of 4a, nor the single crystals of any, for this purpose specially synthesized new bis-(O-acetyl)-(7a), bis-(O-benzoyl)-(7b) and bis-(O-4-acetylaminophenylsulfonyl)-(7c) derivatives, were obtained. However, the configuration of the prepared bis-(dioxein[5,6-c]pyridin-9-ols) 4 was confirmed by the single crystal X-ray diffraction of bis-(dioxein[5,6-c]pyridin-9-ol) 4b monohydrate, showing its racemic but not meso configuration[24] (Figure 1).

The essential crystallographic data of 1a, 1b, 3a maleate salt, as well as those of 3b and 4b monohydrates, are shown in Table II. Full details of their crystal structures are or will be published elsewhere.[19,23,24]
All synthesized bis-dioxepinopyridinols 3 and 4 represent novel pyridoxine intermediates in which they can be easily hydrolyzed in hydrochloric acid.

The significance of this finding is still under investigation.

EXPERIMENTAL

Chemistry. General Information.

Melting points were determined using a Fischer-Johns apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer Model 257 spectrophotometer from a KBr pelleted sample or as film. $^1$H- (300 and 90 MHz) and $^{13}$C- (75 and 25 MHz) NMR spectra were recorded by Varian XL-GEM 300 and Jeol FX 90Q spectrometers, with TMS as internal standard; the values of chemical shifts ($\delta$) are given in ppm and coupling constants ($J$) in Hz; DMSO-$d_6$ was used as solvent unless otherwise stated. Mass spectra were scanned on a Hitachi-Perkin-Elmer RMU-6M instrument operating at 70 eV. TLC was performed using the Merck Kieselgel 60 F$_{254}$ silica plates and components were visualized using UV light (UV 254 nm), iodine vapor and spraying by diazotized sulfanilamide (red spots). Compounds were purified by column chromatography using Merck Kieselgel 60 (0.063–0.200 mm, 70–230 mesh), and were homogeneous by TLC. Solvents p.a. grade were used without further purification. All chemicals, i.e. cis-2-butene-1,4-diol, glyoxal (30% aqueous solution), glutardialdehyde (25% aqueous solution), terephthalaldehyde and 1,1,3,3-tetramethoxypropane for preparing the starting olefins are commercially available and were supplied by Merck. Oxazoles 2a–c were prepared by known procedures.$^{20–22}$ Hydrochinone and 2,6-di-tert-butyl-4-methylphenol were used as antioxidants and p-toluenesulfonic- and perchloric acid, and acetic anhydride as catalysts. The yields were not optimized.

4,7-Dihydro-2-(4,7-dihydro-1,3-dioxepin-2-yl)-1,3-dioxepin (1a)

A mixture of cis-2-butene-1,4-diol (211.2 g, 2.4 mole), aqueous solution of glyoxal (30%, w/w, 193.0 g, 1.0 mole), toluene (160 mL) and p-toluenesulfonic acid (2.7 g) was heated at boiling temperature until complete azeotropic removal of water (about 44 mL). The reaction mixture was cooled and the formed crystals were suction filtered, washed with toluene and dried in vacuo to yield the title compound 1a (110.0 g, 55.6%, m.p. 93–96 °C). After recrystallization from acetone, the sample showed m.p. 100–102 °C. IR (KBr) $v_{\text{max}}$/cm$^{-1}$: 3010m, 2960w, 2940m, 2850m, 1455s, 1395m, 1380s, 1330s, 1270s, 1230s, 1120vs, 1000vs, 950vs, 905w, 830m and 720s.

Anal. Calc. for C$_{10}$H$_{14}$O$_4$ (M$_r$ = 198.22): C 60.59, H 7.12%; found: C 60.77, H 7.33%.

4,7-Dihydro-2-(4,7-dihydro-1,3-dioxepin-2-yl-methyl)-1,3-dioxepin (1b)

A mixture of 1,1,3,3-tetramethoxypropane (82.0 g, 0.5 mole), 88.0 g (1.0 mole) of cis-2-butene-1,4-diol and two drops of concentrated sulfuric acid was slowly warmed up to 115 °C along with simultaneous distillation of the reaction formed methanol. Following the cooling and neutralization by solid sodium carbonate, the reaction mixture was distilled in vacuo to yield the title compound 1b (61.5 g, 58.0%, b.p. 85 °C/ 53.3 Pa). After recrystallization from n-hexane or light petroleum, the samples
showed m.p. 58–59 °C, and 60–61 °C respectively (Ref. 13: Y. = 92.0%, b.p. 100 °C/240 Pa, m.p. 58–59 °C). IR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3040w, 2950m, 2910m, 2870m, 1450s, 1400s, 1370m, 1290m, 1250m, 1205s, 1120vs, 1080vs, 1060s, 1030s, 1010s, 965s, 900s, 870s and 780s.

4,7-Dihydro-2-[3-(4,7-dihydro-1,3-dioxepin-2-yl)-propyl]-1,3-dioxepin (1e)

A mixture of cis-2-butene-1,4-diol (44.0 g, 0.5 mol), 100.0 g (0.25 mol) aqueous solution of glutardialdehyde (25%, w/w), 100 mL toluene and 0.8 g of p-toluenesulfonic acid was heated at boiling temperature until complete azeotropic removal of water. Following the cooling, neutralization by solid sodium carbonate and evaporation of the excess of toluene, the reaction mixture was distilled in vacuo to yield the title compound 1c (50.5 g, 84.1%, b.p. 129–134 °C/26.7 Pa). After recrystallization from n-hexane or light petroleum, the sample showed m.p. 38 °C and 33–34 °C, respectively (Ref. 15: Y. = 80.0%, b.p. 130–133 °C/200 Pa, m.p. 34 °C from pentane; Ref. 14: b.p. 144–146 °C/53.3 Pa, m.p. 37–38 °C). IR (film) $\nu_{\text{max}}$/cm$^{-1}$: 3040m, 2950s, 2870s, 1485s, 1395s, 1275s, 1205s, 1135vs, 1090s, 1015s, 985s, 920m and 845m.

4,7-Dihydro-2-[4-(4,7-dihydro-1,3-dioxepin-2-yl)-phenyl]-1,3-dioxepin (1d)

A mixture of cis-2-butene-1,4-diol (105.6 g, 1.2 mole), 67.1 g (0.5 mole) terephthalaldehyde, 100 mL toluene and 1.4 g of p-toluenesulfonic acid was heated at boiling temperature until complete azeotropic removal of water. The reaction mixture was concentrated under reduced pressure to half volume, cooled and the formed crystals were suction filtered, washed with acetone and dried in vacuo to yield the title compounds 1d (59.6 g, 43.5%, m.p. 119–122 °C). After recrystallization from acetone, the sample showed m.p. 132–133 °C (Ref. 13: m.p. 134–136 °C from benzene). IR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3020m, 2930m, 2900w, 2860m, 1450m, 1425s, 1350vs, 1265s, 1225s, 1115vs, 1085vs, 1040s, 1020s, 1010s, 985m, 945w, 925s, 900s, 800s and 780vs.

General Procedure for the Preparation of 1,5-Dihydro-9-hydroxy-8-methyl-3H-[1,3]-dioxepino[5,6-c]pyridines 3 and 4

This procedure is illustrated by the preparation of 1,5-dihydro-3-(4,7-dihydro-1,3-dioxepin-2-yl)-9-hydroxy-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridine (3a) and 3-(1,5-dihydro-9-hydroxy-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridin-3-yl)-1,5-dihydro-9-hydroxy-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridine (4a). A mixture of bis-dioxepin 1a (1.98 g, 0.01 mol), oxazole 2c (12.96 g, 0.12 mol), p-toluenesulfonic acid (0.03 g) and 2,6-di-tert-butyl-4-methylphenol (0.1 g) was refluxed for 15 hours. The excess of oxazole 2c was removed by distillation under reduced pressure, and purification of the residue by column chromatography using ethyl acetate-methanol mixture under gradient mode as eluent furnished the title compounds 3a and 4a. Mono-duct 3a (0.56 g, 20.1%, m.p. 165–170 °C) was eluted as the first. After recrystallization from ethyl acetate the sample displayed m.p. 177–179 °C. R$_f$ = 0.57 & 0.68 [TLC; Eluents: ethyl acetate-methanol-aq. ammonia (25%) = 20 : 5 : 1 and ethyl acetate-methanol = 4 : 1, respectively; Visualization: UV 254 nm and spraying by diazotized sulfanilamide (red spots)]. IR (KBr) $\nu_{\text{max}}$/cm$^{-1}$: 3500–2300 broad, assoc., 1605w, 1450m, 1420m, 1380m, 1330m, 1260s, 1245s, 1210m, 1130vs, 1060m, 1040m, 1000m, 990m, 945s, 900w, 840w, 810w, 750 w and 710w; MS m/z 279 (4.3%) [M]$^+$, 180 (53.0%), 152
(19.0%), 151 (14.9%), 150 (10.0%), 135 (5.8%), 134 (23.0%), 124 (7.2%), 123 (5.5%), 122 (9.7%), 106 (65.2%), 99 (38.7%), 79 (7.6%), 71 (48.9%) and 43 (100.0%).

Anal. Calcd. for C_{14}H_{17}NO_{5} (M_r = 279.29): C 60.21, H 6.14, N 5.02%; found: C 60.36, H 6.42, N 5.08%.

Continued elution gave the bis-adduct 4a (0.16 g, 4.4%, m.p. 210–213 °C). After recrystallization from absolute ethanol, the sample displayed m.p. 215–217 °C. R_f = 0.09 & 0.16 [for TLC conditions see above]. IR (KBr) v_{max}/cm^{-1}: 3600–2000 broad, assoc., 1590m, 1510m, 1435s, 1410s, 1370s, 1330s, 1280s, 1240vs, 1130vs, 1060s, 990m, 940m, 890m and 700m.

Anal. Calcd. for C_{18}H_{20}N_{2}O_{6}(M_r = 360.37): C 59.99, H 5.59, N 7.77%; found: C 60.36, H 5.86, N 7.42%.

The following were prepared in the same manner:

1,5-Dihydro-3-(4,7-dihydro-1,3-dioxepin-2-yl-methyl)-9-hydroxy-8-methyl-3H-[1,3]-dioxepin[5,6-c]pyridine (3b) and 3-(1,5-Dihydro-9-hydroxy-8-methyl-3H-[1,3]-dioxepin-5,6-c]pyridin-3-yl-methyl)-1,5-dihydro-9-hydroxy-8-methyl-3H-[1,3]-dioxepin[5,6-c]pyridine (4b)

Starting from bis-dioxepine 1b (2.12g, 0.01mol), oxazole 2c (12.96 g, 0.12 mol), acetic anhydride (0.06 g) and hydrochinone (0.03 g) according to the general procedure, bis-dioxepine 3b (1.13 g, 38.5%, m.p. 127–130 °C) was obtained first. After recrystallization from ethyl acetate, the sample showed m.p. 131–133 °C. R_f = 0.70 & 0.74 [for TLC conditions see above]. IR (KBr) v_{max}/cm^{-1}: 3500m, 3400–2000 broad, assoc., 1600m, 1550m, 1490m, 1440s, 1400s, 1370vs, 1350s, 1295s, 1285s, 1260s, 1245s, 1215s, 1130vs, 1100vs, 1080vs, 1050s, 1035s, 1015s, 995s, 950m, 920m, 910m, 860m, 800m, 770m, 705m, 695m, and 635m; MS m/z 293 (4.7%) [M]^+, 180 (7.5%), 152 (42.3%), 151 (100.0%), 135 (19.3%), 134 (14.9%), 124 (9.3%), 123 (29.8%), 122 (27.3%), 106 (47.2%), 99 (6.9%), 79 (6.7%), 71 (42.9%) and 43 (46.0%).

Anal. Calcd. for C_{15}H_{19}NO_{5}(M_r = 293.32): C 61.42, H 6.53, N 4.78%; found: C 61.64, H 6.41, N 4.51%.

Continued elution gave the bis-adduct 4b (0.73 g, 19.5%, m.p. 226–229 °C). After recrystallization from the ethyl acetate-ethanol (4 : 1, v/v) mixture, the sample showed m.p. 231–233 °C. R_f = 0.21 & 0.22 [for TLC conditions see above]. IR (KBr) v_{max}/cm^{-1}: 3500–2500 broad, assoc., 1590s, 1555m, 1520s, 1440s, 1420vs, 1390vs, 1370vs, 1310vs, 1290s, 1240s, 1215s, 1130vs, 1080vs, 1060s, 1020s, 990m, 940w, 875m, 790m and 705m.

Anal. Calcd. for C_{19}H_{22}N_{2}O_{6}(M_r = 374.39): C 60.95, H 5.92, N 7.48%; found: C 60.72, H 5.82, N 7.61%.

1,5-Dihydro-3-[3-(4,7-dihydro-1,3-dioxepin-2-yl)-propyl]-9-hydroxy-8-methyl-3H-[1,3]-dioxepin[5,6-c]pyridine (3c) and 3-[3-(1,5-Dihydro-9-hydroxy-8-methyl-3H-[1,3]-dioxepin[5,6-c]pyridin-3-yl)-propyl]-1,5-dihydro-9-hydroxy-8-methyl-3H-[1,3]-dioxepin[5,6-c]pyridine (4c)

Method A

Starting from bis-dioxepine 1c (2.40 g, 0.01 mol), oxazole 2c (12.96 g, 0.12 mol), acetic anhydride (0.30 g) and hydrochinone (0.1 g) according to the general procedure, bis-dioxepine 3c (0.51 g, 15.9%, m.p. 110–114 °C) was obtained first. After re-
crystallization from ethyl acetate, the sample displayed m.p. 116–118 °C. \( R_f = 0.74 \) & 0.77 [for TLC conditions see above]. IR (KBr) \( \nu_{\text{max}} \text{cm}^{-1} \): 3020w, 2920s, 2860s, 1595s, 1445s, 1375s, 1285s, 1270s, 1185s, 1150sh, 1130vs, 1120vs, 1090s, 1070s, 1010m, 990s and 910m; MS \( m/z \): 321 (11.1%) [M]+, 180 (30.0%), 152 (98.6%), 151 (100.0%), 150 (37.8%), 135 (40.6%), 134 (36.2%), 124 (14.9%), 123 (34.9%), 122 (33.9%), 106 (98.4%), 99 (52.6%), 79 (10.0%), 71 (61.0%) and 43 (85.5%).

**Anal.** Calcd. for C\(_{17}\)H\(_{23}\)NO\(_5\) (\( M_r = 321.37 \)): C 63.54, H 7.21, N 4.36%; found: C 63.71, H 7.04, N 4.59%.

Continued elution gave the bis-adduct 4c (0.21 g, 5.2%, m.p. 157–161 °C). After recrystallization from the ethyl acetate-ethanol (4:1, v/v) mixture, the sample showed m.p. 165–168 °C. \( R_f = 0.27 \) & 0.23 [for TLC conditions see above]. IR (KBr) \( \nu_{\text{max}} \text{cm}^{-1} \): 3600–2500 broad, assoc., 1600s, 1435m, 1415m, 1335m, 1310s, 1280s, 1230s, 1210s, 1140vs, 1120s, 1080m, 1040m, 935m and 860m.

**Anal.** Calcd. for C\(_{21}\)H\(_{26}\)N\(_2\)O\(_6\) (\( M_r = 403.44 \)): C 62.51, H 6.75, N 6.94%; found: C 62.28, H 6.98, N 6.78%.

**Method B**

A mixture of bis-dioxepine 1c (2.40g, 0.01 mol), oxazole 2a (10.0 g, 0.12 mol), nitrobenzene (1.23 g, 0.01 mol), acetic anhydride (0.06 g) and hydrochinone (0.04 g) was heated in a sealed tube at 180–190 °C for 2 hours. After the workup of the reaction mixture according to the general procedure, bis-dioxepin 3c (0.76 g, 23.6%, m.p. 111–115 °C) was obtained first. After recrystallization from ethyl acetate, the sample displayed m.p. 116–118 °C. Its IR spectrum was identical to the spectrum of an authentic sample from procedure A (see above). Continued elution gave the bis-adduct 4c (0.48 g, 11.9%, m.p. 158–161 °C). After recrystallization from the ethyl acetate-ethanol (4:1, v/v) mixture, the sample showed m.p. 165–168 °C. Its IR spectrum was identical to the spectrum of an authentic sample from procedure A (see above).

1,5-Dihydro-3-[4-(4,7-dihydro-1,3-dioxepin-2-yl)-phenyl]-9-hydroxy-8-methyl-3H-[1,3]-dioxepin(5,6-c)pyridine (3d)

Starting from bis-dioxepine 1d (2.74 g, 0.01 mol), oxazole 2b (11.0 g, 0.0865 mol), and hydrochinone (0.1 g) according to the general procedure, only the bis-dioxepin 3d (0.70 g, 19.7%, m.p. 156–160 °C) was obtained. After recrystallization from ethyl acetate, the sample showed m.p. 165–167 °C. \( R_f = 0.77 \) & 0.81 [for TLC conditions see above]. IR (KBr) \( \nu_{\text{max}} \text{cm}^{-1} \): 3400m, 3400–2500 broad, assoc., 1445m, 1420s, 1410s, 1370m, 1360s, 1340vs, 1300m, 1280s, 1260vs, 1240vs, 1220s, 1120vs, 1110vs, 1080vs, 1060s, 1035s, 1010s, 1005s, 955m, 920w, 890s, 790s, 775vs, 700w and 625s; MS \( m/z \): 355 (100.0%) [M]+, 180 (2.0%), 152 (9.9%), 151 (45.5%), 150 (20.4%), 135 (100.0%), 134 (6.5%), 124 (4.1%), 123 (26.7%), 122 (17.4%), 106 (19.1%), 99 (3.0%), 79 (10.9%), 71 (6.8%) and 43 (9.0%).

**Anal.** Calcd. for C\(_{29}\)H\(_{21}\)NO\(_5\) (\( M_r = 355.39 \)): C 67.59, H 5.96, N 3.94%; found: C 67.31, H 6.12, N 4.22%.

Their structures were consistent with analytical and spectral data (Table I) and were confirmed by the X-ray analysis data (Table II and Figure 1).
General Procedure for the Preparation of
1,5-Dihydro-9-hydroxy-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridines 4a–c
from Dioxepino[5,6-c]pyridin-9-ols 3

This procedure is illustrated by the preparation of 3-(1,5-dihydro-9-hydroxy-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridin-3-yl)-1,5-dihydro-9-hydroxy-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridine (4a). A mixture of 1,5-dihydro-9-hydroxy-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridine 3a (2.97 g, 0.01 mol), oxazole 2c (38.5 g, 0.356 mol), p-toluene-sulfonic acid (0.05 g) and 2,6-di-tert-butyl-4-methylphenol (0.1 g) was refluxed for 48 hours. The excess of oxazole 2c was removed by distillation under reduced pressure, and purification of the residue by column chromatography using the ethyl acetate-methanol mixture under gradient mode as eluent furnished the unreacted 3a (0.55 g, 18.5%, m.p. 172–176 °C) and the title compound 4a (1.20 g, 33.3%, m.p. 208–212 °C). After recrystallization from absolute ethanol, the sample showed m.p. 215–217 °C. Its IR spectrum was identical to the spectrum of an authentic sample prepared as above.

The following were prepared in the same manner:

3-(1,5-Dihydro-9-hydroxy-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridin-3-yl-methyl)-1,5-dihydro-9-hydroxy-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridine (4b)

A mixture of bis-dioxepine 3b (2.93 g, 0.01 mol), oxazole 2c (19.44 g, 0.18 mol), acetic anhydride (0.20 g) and hydrochinone (0.1 g) was refluxed for 8 hours and after the workup of the reaction mixture according to the general procedure, unreacted 3b (1.38 g, 47.1%, m.p. 126–129 °C) and the title compound 4b (0.57 g, 15.2%, m.p. 225–229 °C) were obtained. After recrystallization from the ethyl acetate absolute ethanol mixture (4/1), the 4b sample showed m.p. 231–233 °C. Its IR spectrum was identical to the spectrum of an authentic sample prepared as above.

3-[3-(1,5-Dihydro-9-hydroxy-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridin-3-yl)-propyl]-1,5-dihydro-9-hydroxy-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridine (4c)

A mixture of bis-dioxepine 3c (3.21 g, 0.01 mol), oxazole 2c (43.3 g, 0.40 mol), acetic anhydride (0.30 g) and hydrochinone (0.1 g) was refluxed for 18 hours. After the workup of the reaction mixture according to the general procedure, unreacted 3c (0.82 g, 10.0%, m.p. 112–115 °C) and the title compound 4c (0.64 g, 15.8%, m.p. 159–162 °C) were obtained. After recrystallization from the ethyl acetate absolute ethanol mixture (4/1), the 4c sample showed m.p. 165–168 °C. Its IR spectrum was identical to the spectrum of an authentic sample prepared as above.

5-Chloromercury-2-(4,7-dihydro-1,3-dioxepin-2-yl)-6-nitro-1,3-dioxepane (5)

To the solution of mercury(II) chloride (6.9 g, 0.025 mol) and sodium nitrite (3.5 g, 0.050 mol) in 75 mL water, the bis-dioxepine 1a (5.0 g, 0.025 mol) was added in small portions for 1 hour. The mixture was stirred at room temperature for 24 hours and the formed precipitate was filtered, washed with water and dried under vacuo at room temperature to give the nitromercurial 5 (10.0 g, 82.8%, m.p. 160 °C decompn.). IR (KBr) νmax cm⁻¹: 3050w, 2940m, 2895m, 2860m, 1625w, 1550vs, 1460s, 1395s, 1360s, 1330s, 1285s, 1205m, 1120vs, 1020vs, 930, 820s, 785s, 720m and 640s.
4,7-Dihydro-2-(4,7-dihydro-1,3-dioxepin-2-yl)-5-nitro-1,3-dioxepin (6)

To the suspension of nitromercurial 5 (5.0 g, 0.010 mol) in 50 mL of dichloromethane, aqueous sodium hydroxide solution (4.2 mL, c = 2.5 mol L⁻¹) was added dropwise under vigorous stirring at room temperature for 1 hour. The reaction mixture was stirred at the same temperature for further 30 minutes. After addition of diatomaceous earth (2.0 g), the precipitated elementary mercury was filtered off. The dichloromethane layer was washed with water, dried over anhydrous sodium sulfate and concentrated furnishing the crude 6 (1.6 g, 62.9%, m.p. 109–111 °C). After recrystallization from ethylacetate the sample showed m.p. 113–114 °C. IR (KBr) \( \nu_{\text{max/cm}^{-1}} \): 3090w, 3035w, 2950m, 2850m, 1680m, 1525vs, 1445m, 1390m, 1345vs, 1285m, 1275m, 1260m, 1250m, 1120vs, 1015s, 985m, 965m, 870w, 820w, 800m, 705m and 690m; \(^1\)H-NMR (DMSO-\(d_6\)) \( \delta \): 7.37 (t, 1H, \( J = 3.4 \), H-C6); 5.70 (s, 2H, H-C5’,6’); 4.99–4.67 (m, 6H, H-C4,7 & 2,2’); 4.43 & 4.17 (dd, 4H, \( J = 15.3 \), H-C4’,7’); \(^{13}\)C-NMR \( \delta \): 149.88 (C5), 138.04 (C6), 129.44 (C5’,6’), 100.59 & 100.54 (C2 & 2’), 65.84 (C4’,7’), 62.46 & 61.83 (C7’&4’).

Anal. calcld. for C\(_{10}\)H\(_3\)N\(_2\)O\(_6\) (\( M_r = 243.22 \)): C 49.38, H 5.39, N 5.76%; found: C 49.50, H 5.69, N 5.66%.

1,5-Dihydro-3-(4,7-dihydro-1,3-dioxepin-2-yl)-9-hydroxy-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridine (3a) from 6

A mixture of nitro-bis-dioxepin 6 (1.00 g, 0.004 mol), oxazole 2a (7.00 g, 0.084 mol) and catalytic amount of perchloric acid was refluxed for 4 hours. The excess of oxazole 2a was removed by distillation under reduced pressure, and purification of the residue by column chromatography using the ethyl acetate-acetone (1 : 1) mixture as eluent furnished 3a (0.31 g, 27.7%, m.p. 164–165 °C) and some other products. After recrystallization from ethylacetate the sample showed m.p. 177–179 °C. Its IR spectrum was identical to the spectrum of an authentic sample prepared as above.

1,5-Dihydro-3-(4,7-dihydro-1,3-dioxepin-2-yl)-9-hydroxy-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridine Maleate Salt (3a × maleic acid)

To the solution of bis-dioxepine 3a (0.60 g, 2.15 mmol) in 10 mL of methanol, a solution of maleic acid (0.20 g, 1.72 mmol) in 3.5 mL of methanol was added, furnishing after two days standing at room temperature the 3a mono maleate salt (0.52 g, 61.2%, m.p. 193–197 °C). After recrystallization from methanol-water mixture, the sample showed m.p. 198–200 °C. IR (KBr) \( \nu_{\text{max/cm}^{-1}} \): 3600–1900 broad, assoc., 1580s, 1470vs, 1395s, 1340vs, 1280s, 1265vs, 1245m, 1210m, 1180s, 1140vs, 1090vs, 1020vs, 980s, 930m, 910s, 895s, 880s, 800s 750s and 710s.

Anal. Calcd. for C\(_{19}\)H\(_{22}\)N\(_2\)O\(_9\) (\( M_r = 395.37 \)): C 54.68, H 5.35, N 3.55%; found: C 54.41, H 5.60, N 3.51%.

3-(9-Acetoxy-1,5-dihydro-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridin-3-yl)-9-acetoxy-1,5-dihydro-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridine (7a)

A mixture of bis-dioxepinoypyridinol 4a (0.36 g, 0.001 mol), acetic anhydride (7.0 g, 0.0686 mol) and pyridine (7.0 g, 0.0885 mol) was stirred at room temperature for 22 hours. Methanol (10 mL) was carefully added to the reaction mixture under cooling, and the mixture was concentrated under reduced pressure to dryness. The procedure was repeated two more times furnishing the crude 7a (0.38 g, 86.4%, m.p.
>250 °C). After two recrystallizations from methyl-ethyl-ketone the sample showed m.p. 260–262 °C. IR (KBr) $v_{\text{max/cm}^{-1}}$: 2970w, 2880w, 2850w, 1740vs, 1590m, 1440s, 1400s, 1370s, 1275s, 1220s, 1200vs, 1160s, 1070s, 1110s, 985s, 980s, 885m, 800w, 760w and 710w.

*Anal.* Calcd. for C$_{22}$H$_{24}$N$_{2}$O$_{8}$ ($M_r = 444.44$): C 59.45, H 5.44, N 6.30%; found: C 59.21, H 5.59, N 6.18%.

3-(9-Benzoyloxy-1,5-dihydro-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridin-3-yl)-9-benzoyloxy-1,5-dihydro-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridine (7b)

To the refluxed mixture of bis-dioxepinopyridinol 4a (0.36 g, 0.001 mol) and potassium tert-butoxide (0.22 g, 0.002 mol) in tetrahydrofurane (20 mL), the solution of benzoyl-chloride (0.28 g, 0.002 mol) in tetrahydrofurane (5 mL) was added dropwise for 30 minutes, and the mixture was refluxed for further 30 minutes. The reaction mixture was cooled to room temperature, pH was adjusted to 7 by addition of small quantities of powdered potassium tert-butoxide and the mixture was concentrated under reduced pressure. Purification of the residue by column chromatography using ethyl acetate methanol mixture under gradient mode as eluent furnished the title compound 7b (0.28 g, 49.3%, m.p. 240–245 °C). After recrystallization from ethyl acetate the sample showed m.p. 249–251 °C. IR (KBr) $v_{\text{max/cm}^{-1}}$: 3050w, 2860m, 1740vs, 1590s, 1440s, 1400m, 1360s, 1310m, 1260vs, 1200vs, 1175s, 1120vs, 1085vs, 1070vs, 1020s, 1000m, 930s, 880m, 800w and 755s.

*Anal.* Calcd. for C$_{32}$H$_{28}$N$_{2}$O$_{8}$ ($M_r = 568.58$): C 67.60, H 4.96, N 4.93%; found: C 67.38, H 5.13, N 5.17%.

3-(9-(4-Acetylamino phenyl sulfonyloxy)-1,5-dihydro-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridin-3-yl)-9-(4-acetylamino phenyl sulfonyloxy)-1,5-dihydro-8-methyl-3H-[1,3]dioxepino[5,6-c]pyridine (7c)

To the refluxed mixture of bis-dioxepinopyridinol 4a (0.36 g, 0.001 mol) and potassium tert-butoxide (0.22 g, 0.002 mol) in tetrahydrofurane (20 mL), the solution of 4-acetylamino benzenesulfonyl-chloride (0.47 g, 0.002 mol) in tetrahydrofurane (5 mL) was added dropwise for 30 minutes, and the mixture was refluxed for further 30 minutes. The reaction mixture was cooled to room temperature, pH was adjusted to 7 by addition of small quantities of powdered potassium tert-butoxide and the mixture was concentrated under reduced pressure. Purification of the residue by column chromatography using ethyl acetate methanol mixture under gradient mode as eluent furnished the title compound 7c (0.40 g, 53.1%, m.p. 178–183 °C). After recrystallization from ethyl acetate, the sample showed m.p. 184–186 °C. IR (KBr) $v_{\text{max/cm}^{-1}}$: 3500m, 3320–2860 assoc, 1690s, 1590vs, 1530s, 1500sh, 1400s, 1360vs, 1320s, 1270s, 1210vs, 1180vs, 1130s, 1110s, 985m, 940m, 900m, 850m, 820m, 780sh and 770vs.

*Anal.* Calcd. for C$_{34}$H$_{34}$N$_{4}$O$_{12}$S$_{2}$ ($M_r = 754.78$): C 54.10, H 4.54, N 7.42%; found: C 53.91, H 4.28, N 7.55%.

Acknowledgment. – We are grateful to Dr. Mladen Proštenik for valuable discussions and Prof. J. Seibl for the MS spectra measurement. The generous financial support by the Ministry of Science and Technology of the Republic of Croatia is highly appreciated.
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17. Known for a long time the acetalization of glyoxal by dihydric alcohols can occur in either of the two directions (A and/or B) accompanied by oligomerization; see P. P. Castro, S. Tihomirov, and C. G. Gutierrez, J. Org. Chem. 53 (1988) 5181 and Ref. 18.

![Scheme 2.](image)

The obtained spectral analyses speak well for both of the proposed structures. X-ray diffraction of 1a sample solved the dilemma and showed that the A direction was right.

**SAŽETAK**

*Kemija 1,3-dioksepina. XI. Bis-(4,7-dihidro-1,3-dioksepin)-pristup do 1,5-dihidro-8-metil-3H-[1,3]dioksepino[5,6-c]piridin-9-ola, međuprodukata u sintezi piridoksina*

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Novi bis-dioksepino[5,6-c]piridin-9-oli 3 i 4, međuprodukti u sintezi piridoksina, sintetizirani su iz bis-(4,7-dihidro-1,3-dioksepina) 1. Njihova konstitucija i konfiguracija povrđena je rentgenskom strukturnom analizom monokristala bis-dioksepina 1a i 1b, maleata dioksepinopiridinola 3a te monohidrata dioksepinopiridinola 3b i 4b.