We now describe a convenient procedure for the synthesis of different carbohydrate methylene acetics using dibromomethane as the reagent in dimethyl sulfoxide in the presence of fine powdered potassium hydroxide. Application of this system has been found particularly useful for the alkylation of carbohydrate derivatives.5

Our procedure covers the methylation of 2,3-di-O-alkylhexopyranosides (1a-d) in the 4,6-positions and the pentofuranoside (1e) in the 3,5-positions to give dioxane-type methylene derivatives (2a-e). The trans-diequatorial hydroxy groups in compounds 1f and 1g, and the cis-axial-equatorial hydroxy groups in compounds 1h-j are transformed into dioxolane-type methylene acetics (2f-j) in the methylation reaction. In all reaction mixtures the different isomers of the dimers could be also detected by T.L.C., but their quantity did not exceed 5-8%, so we did not attempt their isolation. The I.R. spectra of the compounds did not show hydroxy-stretching frequencies, confirming their entire protection. On the basis of the $^1$H-N.M.R. spectra, the compounds can be divided into three groups. In the spectra of the dioxane-type methylene derivatives (2a-e) the axial proton of the dioxane ring resonates at a lower field than the equatorial one, and the value of the geminal coupling constant is about 6.5 Hz. In the case of the dioxolane-type methylene derivatives, involving trans-diequatorial hydroxy groups (2f, g), the two hydrogens of the methylene group give one sharp singlet whereas two distinct singlets were observed for the methylene protons of those dioxolane derivatives (2h-j) which are formed from cis-axial-equatorial hydroxy groups. The low-field signals can be assigned to the endo-hydrogens, and the high-field signals belong to the exo ones.

Optical rotations were measured with a Perkin-Elmer Model 241 automatic polarimeter at room temperature. I.R. spectra were recorded on a Perkin-Elmer 700 spectrophotometer. $^1$H-N.M.R. spectra were obtained on a JEOL-MH-100 (100 MHz) instrument with TMS as the internal standard. T.L.C. examination was carried out on DC-Alufol Kieselgel 60F 254 (Merck) layer, and the detection was performed with 50% sulfuric acid.

**Phenyl 2,3-Di-O-benzyl-4,6-O-methylene-beta-D-galactopyranoside (2a)**

**Typical Procedure:**

A mixture of phenyl 2,3-di-O-benzyl-4,6-O-methylene-beta-D-galactopyranoside6 (1a; 2.18 g, 0.005 mmol), finely powdered potassium hydroxide (2.24 g, 0.04 mol) and dibromomethane (1.74 g, 0.01 mol) is suspended in dry dimethyl sulfoxide (10 ml) and the mixture is stirred at room temperature. The reaction is monitored by T.L.C., performed on Kieselgel layer with 95:5 dichloromethane/acetone as eluent. After the starting material has disappeared (1 2 h) the reaction mixture is diluted with dichloromethane (50 ml), filtered, the filtrate is washed with water (5 x 20 ml), dried with sodium sulfate, and the solvent removed under reduced pressure. The residue is crystallized from ethyl acetate/cyclohexane: yield: 1.10 g (49%); m.p. 178-180°C; $[\alpha]_D^{20}$ = -44.3° (c 0.60, chloroform); Rf: 0.81.  

C$_{21}$H$_{28}$O$_7$  
calc. C 72.30  
(448.5)  
found 72.41  
H 6.29  
6.35

**Oligosaccharide antibioticos**12,13 of the orthosomycin family contain 2,3-O-methylene-aldonolactones of different configurations and this finding has initiated new efforts for the synthesis of suitable methylene acetics14.

---

**A Convenient Synthesis of Carbohydrate Methylene Acetics**

András Lipták*, V. Anna Oláh, János Kereckvártó

Institute of Biochemistry, Kossuth L. University, 4010-Debrecen, Hungary

Acetylation is one of the most useful reactions in carbohydrate chemistry for the synthesis of partially blocked derivatives. While the acid-catalyzed acetylation and trans-acetylation reactions are the most common procedures for the preparation of different acetics, these reactions result only in very poor yield in the case of methylene derivatives. Several attempts have been made to produce the desired derivatives under alkaline conditions; Brimacombe et al.5 used sodium hydride/dibromo- or dichloromethane in dimethylformamide and isolated dioxolane derivatives involving vicinal cis- and trans-diols. Hanessian et al.6,7, and more recently Munavvu5, used dimethyl sulfoxide/N-bromosuccinimide or dimethyl sulf oxide/bromine systems for the preparation of methylene acetics utilizing the Pummerer rearrangement of an initially formed bromosulphonium ion to give an α-alkoxy sulfoxide intermediate. Phase-transfer catalysis also proved to be a very useful method for the methylation of catechol, and this procedure was applied by Cesare and Gross8, as well, in the field of carbohydrates for obtaining cis-fused methylene derivatives. The preparation of trans-fused methylene acetics under phase-transfer conditions was successfully achieved by Kim and Szarek11.

Oligosaccharide antibioticos12,13 of the orthosomycin family contain 2,3-O-methylene-aldonolactones of different configurations and this finding has initiated new efforts for the synthesis of suitable methylene acetics14.
<table>
<thead>
<tr>
<th>Substrate (Reference)</th>
<th>Product</th>
<th>Yield [%]</th>
<th>m.p. [°C] (solvent)</th>
<th>[α]d (c, CHCl₃)</th>
<th>Rf (solvent)</th>
<th>Molecular Formula</th>
<th>H-NMR (CDCl₃/TMS) δ [ppm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1b¹¹</td>
<td>2b</td>
<td>37</td>
<td>118–119° (c-C₆H₅)</td>
<td>0.56</td>
<td>C₉H₁₈O₅</td>
<td>3.43 (dd, H-3, J = 10.1 Hz, 7.3 Hz); 3.90 (dd, H-2, J = 8.0 Hz, 10.1 Hz); 4.44 (d, H-1, J = 8.9 Hz, 4.68 (d, H-1, J = 6.4 Hz, OCH₃-(eq)); 5.18 (d, H-1, J = 6.4 Hz, OCH₃-(ax)); 7.3 m, 15°H-3, 1H-2, 1H-1, J = 6.4 Hz, OCH₃(ax)O)</td>
<td></td>
</tr>
<tr>
<td>1c¹²</td>
<td>2c</td>
<td>44°</td>
<td>87° (C₆H₅OH)</td>
<td>0.61</td>
<td>C₉H₁₈O₅</td>
<td>3.43, 3.53, 3.62 (5s, 9H, OCH₃); 4.14 (dd, H-2, J = 3.6 Hz, 10.0 Hz); 4.59 [d, 1H, J = 6.4 Hz, OCH₃(eq)]; 4.82 [d, H-1, J = 4.0 Hz]; 5.07 [d, 1H, J = 6.4 Hz, OCH₃(ax)O]</td>
<td></td>
</tr>
<tr>
<td>1d¹³</td>
<td>2d</td>
<td>48</td>
<td>syrup</td>
<td>0.76</td>
<td>C₉H₁₈O₅</td>
<td>3.21 (s, 3H, OCH₃); 3.5 (m, H-6(6′)); 3.7 (m, H-5); 3.94 (t, H-3); 4.08 (dd, H-2); 4.52 [d, 1H, J = 6.0 Hz, OCH₃(eq)]; 4.58 (d, H-1, J = 1.9 Hz); 4.7 (m, CH₂CH₂); 4.80 (s, CH₃CH₂); 5.03 [d, 1H, J = 6.0 Hz, OCH₃(ax)O]; 7.2–7.4 (m, 10°H-3, 1H-2, 1H-1, J = 4.5 Hz)</td>
<td></td>
</tr>
<tr>
<td>1e³⁰</td>
<td>2e</td>
<td>72</td>
<td>119–120° (c-C₆H₅)</td>
<td>0.60</td>
<td>C₉H₁₈O₅</td>
<td>3.49, 3.52 (2s, 6H, OCH₃); 4.65 [d, 1H, J = 6.5 Hz, OCH₃(eq)]; 5.09 [d, 1H, J = 6.5 Hz, OCH₃(ax)O]; 5.32 [d, H-1, J = 4.5 Hz)</td>
<td></td>
</tr>
<tr>
<td>1f²¹</td>
<td>2f</td>
<td>48</td>
<td>106–107° (C₆H₅OH)</td>
<td>0.79</td>
<td>C₉H₁₈O₅</td>
<td>3.48 (s, 3H, OCH₃); 5.10 (d, H-1, J = 3.0 Hz); 5.16 (s, OCH₃O); 5.58 (s, CH₃CH₂); 7.4 (m, 5°H-3, 1H-2, 1H-1, J = 4.5 Hz)</td>
<td></td>
</tr>
<tr>
<td>1g²²</td>
<td>2g</td>
<td>36°</td>
<td>181–182° (c-C₆H₅/</td>
<td>0.70</td>
<td>C₉H₁₈O₅</td>
<td>3.4 (m, H-5); 3.39 (dd, H-3, J = 2.4 Hz, 10.0 Hz); 4.00 (dd, H-2, J = 10.0 Hz, 8.0 Hz); 4.10 (dd, H-6, J = 12.8 Hz, 2.0 Hz); 4.40 (dd, H-6′, J = 12.8 Hz, 2.0 Hz); 4.50 (dd, H-4, J = 2.4 Hz, 1.4 Hz); 4.80 (d, H-1, J = 8.0 Hz); 4.9 (m, CH₃CH₂); 5.10 (s, OCH₃O); 5.55 (s, CH₃CH₂); 7.2–7.4 (m, 10°H-3, 1H-2, 1H-1, J = 4.5 Hz)</td>
<td></td>
</tr>
<tr>
<td>1h²³</td>
<td>2h</td>
<td>89</td>
<td>96° (c-C₆H₅)</td>
<td>0.70</td>
<td>C₉H₁₈O₅</td>
<td>3.40 (dd, H-3, J = 9.0 Hz, 5.8 Hz); 3.7–3.9 (m, H-5,6,6′); 4.22 (dd, H-1, J = 8.5 Hz, 9.0 Hz); 4.56 (s, CH₃CH₂); 4.8 (m, 4H, CH₂CH₂); 4.93 (d, H-1, J = 8.5 Hz); 4.97 (s, 1H, OCH₃(eq)); 5.08 (s, 1H, OCH₃(ax)O); 7.2–7.4 (m, 15°H, 1H-2, 1H-1, J = 4.5 Hz)</td>
<td></td>
</tr>
<tr>
<td>1i²⁴</td>
<td>2i</td>
<td>76°</td>
<td>syrup</td>
<td>0.82</td>
<td>C₉H₁₈O₅</td>
<td>3.44 (dd, H-3, J = 7.8 Hz, 4.1 Hz); 3.8–4.1 (m, 5H, H-4,4′,4′); 5.85 (s, H, CH₃CH₂); 4.32 (dd, H-2, J = 2.9 Hz, 7.8 Hz); 4.7 (m, CH₃CH₂); 4.93 (d, H-1, J = 2.9 Hz); 4.96 (s, 1H, OCH₃(eq)); 5.17 (s, 1H, OCH₃(ax)O); 5.2 (m, CH₃CH₂); 5.9 (m, CH₃CH₂); 7.3–7.4 (m, 5°H-3, 1H-2, 1H-1, J = 4.5 Hz)</td>
<td></td>
</tr>
<tr>
<td>1j²⁵</td>
<td>2j</td>
<td>44°</td>
<td>syrup</td>
<td>0.78</td>
<td>C₉H₁₈O₅</td>
<td>1.28 (d, CH₂, J = 6.5 Hz); 3.13 (dd, H-4, J = 6.9 Hz, 9.5 Hz); 3.35 (s, OCH₃), 3.7 (m, H-5); 3.88 (dd, H-2, J = 1.7 Hz, 5.6 Hz); 4.31 (dd, H-3, J = 5.6 Hz, 6.9 Hz); 4.8 (m, CH₃CH₂); 4.90 (s, H-1, J = 4.9 Hz, 1H, OCH₃(eq)); 5.14 (s, 1H, OCH₃(ax)O); 7.2–7.4 (m, 5°H-3, 1H-2, 1H-1, J = 4.5 Hz)</td>
<td></td>
</tr>
</tbody>
</table>

* Satisfactory microanalyses obtained: C ± 0.34, H ± 0.16.
* Purified by column chromatography.

Lit.¹⁵, m.p. 118–119° (ethanol); [α]d = +123° (c 0.23, CHCl₃).
Lit.¹⁶, m.p. 104–105° (ether); [α]d = +122.9° (c 0.21, CHCl₃).
Compounds 2b-j were prepared similarly and purified by crystallization or chromatography on a Kieselgel G column using the short column technique and eluting with the same solvent as for the T.L.C. analysis (Table).

Received: November 10, 1981

References: