A rapid and convenient synthesis of $\alpha$ and $\beta$ forms of acetylated derivatives of sugars under microwave irradiation

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In a novel method, the synthesis of $\alpha$ and $\beta$ forms of penta as well as octa acetyl derivatives of several sugars under microwave irradiation with improved yields is described.

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Acetylation is among one of the most important reactions employed in carbohydrate chemistry. The commonly used and well established protocol involve the use of acetic anhydride (Ac$_2$O) to carry out acetylation$^1$. The hydroxyl groups at both the anomic and non-anomic carbon atoms can be readily acetylated. The reaction has to be carried out in presence of H$_2$SO$_4$ or pyridine$^3$. But, the acetylation of D-glucose in presence of zinc chloride (ZnCl$_2$) gives the penta acetate 1,2,3,4,6-penta-O-acetyl-$\alpha$-D-glucopyranose. Similarly, the corresponding $\beta$-anomer can be obtained when the reaction is carried by the Libermann’s method using sodium acetate (CH$_3$COONa)$^4$. Further, the heating of $\beta$-anomer in presence of Ac$_2$O/ZnCl$_2$ results in its conversion to the corresponding $\alpha$-anomer$^7$. All these reactions, conventionally, have to be carried out using ten equivalents of Ac$_2$O on a boiling water bath for about 1-2 hr to isolate the penta acetate derivative in about 56 to 72% yield$^6$.

Microwave-assisted reactions have attracted much interest because of the simplicity in operation, greater selectivity and rapid synthesis of a variety of organic compounds$^{7-11}$. The effects usually observed are 1) enhanced reaction rates, 2) formation of pure products in high yields and 3) cleaner reactions with easier work-up. Some of the microwave-assisted reactions reported in the carbohydrate synthesis include the reactions of phenols and alcohols with tri-O-acetyl-D-glucal$^{12}$, saponification of peracetylated glycosides using KOH impregnated onto alumina in dry media$^{13}$, etc. The direct acetylation of primary, secondary alcohols and phenols using zeolites HSZ-360$^{14}$ as well as microwave-mediated acetylation using Ac$_2$O in presence of iodine or montmorillonite k-10$^{15}$ have also been described. Acetylation of hydroxy, thiol and amino groups in solvent free conditions employing Ac$_2$O-pyridine over basic alumina under microwave-irradiation have been described recently$^{16}$.

We report herein the synthesis of $\alpha$ and $\beta$ forms of penta- and octa-acetylated derivatives of sugars under microwave-irradiation (Scheme I). The reactions were carried out in a commercial, unmodified domestic LG make microwave oven (2450 MHz) at 60% of its power. In a typical reaction$^{17}$, a mixture of d-glucose, Ac$_2$O (six equivalents) and CH$_3$COONa (two equivalents) in a conical flask was placed in a microwave oven and irradiated for 10 sec to yield $\beta$-anomer of 1,2,3,4,6-penta-O-acetyl-D-glucopyranose. The use of ZnCl$_2$ (0.25 equivalent) in place of CH$_3$COONa resulted in the isolation of the $\alpha$-anomer. Also, the irradiation of $\beta$-anomer in presence of Ac$_2$O (six equivalents) -ZnCl$_2$ (0.25 equivalents) lead to its conversion to the $\alpha$-anomer. In all the three cases, about 75 to 94% of the product was isolated (Table I), which is about 20-30% increase in yield when compared with the literature yield$^6$. In the case of the conventional and routinely employed procedure under thermal heating, the reaction mixture has to be heated to about 80-100°C for 1-2 hr. In the present protocol, the reaction was found to be complete in 10 sec in the case of $\alpha$-anomer and 20 sec in the case of $\beta$-anomer (Figure 1).

The versatility of the procedure was further demonstrated by the preparation of acetate derivatives of another seven sugars (Table I). As tested for several times, the scale-up of this procedure in the...
PATIL et al.: SYNTHESIS OF α AND β FORMS OF ACETYLATED SUGARS UNDER MW IRRADIATION

2: 1,2,3,4,6-penta-O-acetyl-β-D-glucopyranose; 3: 1,2,3,4,6-penta-O-acetyl-α-D-glucopyranose

Scheme I — Preparation of α and β forms of 1,2,3,4,6-penta-O-acetyl-D-glucopyranose

Table I — Conversion of sugars to the corresponding penta or octa acetyl derivatives under microwave irradiation

<table>
<thead>
<tr>
<th>Compd</th>
<th>Form</th>
<th>Method</th>
<th>Time (sec)</th>
<th>mp(°C)</th>
<th>[α]D (°) (c=1, CHCl₃)</th>
<th>Yield (%)</th>
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<tbody>
<tr>
<td>penta-O-acetyl-β-D-glucopyranose</td>
<td>α</td>
<td>A</td>
<td>15</td>
<td>112</td>
<td>112-14</td>
<td>102</td>
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<td></td>
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<td>B</td>
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<td>133</td>
<td>132-35</td>
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<tr>
<td></td>
<td>α</td>
<td>C</td>
<td>15</td>
<td>113</td>
<td>112-14</td>
<td>102</td>
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<tr>
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<td>95</td>
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Method A: sugar, Ac₂O, ZnCl₂; Method B: penta and octa-acetyl-β-D-sugars, Ac₂O and ZnCl₂; Method C: sugar, Ac₂O and CH₃COONa. *All the compounds were satisfactorily characterized by 1H NMR spectroscopy. **Isolated yield after crystallization.
Experimental Section

Melting points were determined using capillary method and are uncorrected. LG domestic microwave oven operating at 2450 MHz was used for the preparation of acetyl derivatives of sugars. Specific rotations were recorded on a Rudolf Research Autopol IV automatic polarimeter.

General procedure for the preparation of pentaocta-O-acetyl derivatives of sugar

Method A. A mixture of anhydrous ZnCl₂ (0.25 mmole), Ac₂O (6 mmole) in a conical flask was exposed to microwave irradiation for 5 sec and then α-D-glucose (1 mmole) was added and continued the exposure to microwaves till the completion of the reaction. The resulting solution was poured onto 100 mL of ice-water under stirring. The separated solid was filtered, washed with water and recrystallized using ethanol to get the title compound.

Method B. A mixture of sugar (1 mmole), CH₃COONa (2 mmole) and Ac₂O (6 mmole) in a conical flask was exposed to microwave irradiation. After completion of the reaction, the resulting clear solution was worked up as described in the method A.

Method C. A mixture of anhydrous ZnCl₂ (0.25 mmole), Ac₂O (6 mmole) in a conical flask was exposed to microwave irradiation for 5 sec and then penta or octa-O-acetyl-β-sugar (1 mmole) was added and continued the exposure to microwaves till the reaction was complete. It was worked up as described in the method A.

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References