



**HAL**  
open science

# Lewis-Acidic Polyoxometalates as Reusable Catalysts for the Synthesis of Glucuronic Acid Esters under Microwave Irradiation

Michael Bosco, Stéphanie Rat, Nathalie Dupré, Bernold Hasenknopf, Emmanuel Lacôte, Max Malacria, Pauline Rémy, Jose Kovensky, Serge Thorimbert, Anne Wadouachi

## ► To cite this version:

Michael Bosco, Stéphanie Rat, Nathalie Dupré, Bernold Hasenknopf, Emmanuel Lacôte, et al.. Lewis-Acidic Polyoxometalates as Reusable Catalysts for the Synthesis of Glucuronic Acid Esters under Microwave Irradiation. *ChemSusChem*, 2010, 3 (11), pp.1249-1252. 10.1002/cssc.201000218 . hal-04315445

**HAL Id: hal-04315445**

**<https://hal.science/hal-04315445>**

Submitted on 30 Nov 2023

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

# Lewis Acidic Polyoxometalates as Reusable Catalysts for the Synthesis of Glucuronic acid Esters under Microwave Irradiation

Michael Bosco,<sup>[a]</sup> Stéphanie Rat,<sup>[a]</sup> Nathalie Dupré,<sup>[b]</sup> Bernold Hasenknopf,<sup>[b]</sup> Emmanuel Lacôte,<sup>[b]</sup> Max Malacria,<sup>[b]</sup> Pauline Rémy,<sup>[b]</sup> Jose Kovensky,<sup>[a]</sup> Serge Thorimbert,<sup>\*[b]</sup> and Anne Wadouachi<sup>\*[a]</sup>

---

[a] *Dr. M. Bosco, Dr S. Rat, Prof. J. Kovensky, Dr. A. Wadouachi*  
*Université de Picardie Jules Verne, Laboratoire des Glucides UMR CNRS 6219, 33 rue Saint Leu, 80039 Amiens cedex, France*  
*Fax : (+)33 3 22 82 75 60*  
*E-mail: anne.wadouachi@u-picardie.fr*

[b] *N. Dupré, Prof. B. Hasenknopf, Dr. E. Lacôte, Prof. M. Malacria, Dr. P. Rémy, Dr. S. Thorimbert*  
*UPMC Univ Paris 06*  
*Institut Parisien de Chimie Moléculaire (UMR 7201)*  
*C. 229, 4 place Jussieu, 75005 Paris, France*  
*Fax: (+)33 1 44 27 30 56*  
*E-mail: serge.thorimbert@upmc.fr,*

*Dedicated to the memory of the late Professor Marc Julia who passed away on 29 June 2010*

D-Glucuronic acid (GlcA) is an ubiquitous compound of oligo- and polysaccharides of biological importance. GlcA derivatives have been prepared for several applications, as surface-active compounds<sup>[1,2]</sup> or as bioactive molecules.<sup>[3]</sup> Glucuronidation is a well-known drug-metabolizing reaction and is generally regarded as a detoxification process. Glucopyranuronate derivatives have been used as glycosyl donors for glucuronidation of pharmacological active compounds to form synthetic glucuronides which were compared to natural metabolites.<sup>[4]</sup> Recently the synthesis of non-toxic prodrugs has been extensively studied as a strategy in cancer therapy for application in Antibody Directed Enzyme Prodrug Therapy (ADEPT)<sup>[5]</sup> or in Prodrug Monotherapy (PMT).<sup>[6]</sup> These prodrugs are synthesized for the most from imidate glucuronate derivatives or ester glucuronates with free anomeric hydroxyls.

Esters are important industrial products, obtained commonly by condensation between carboxylic acids (or their derivatives) and alcohols, transesterification of methyl or ethyl esters and alkylation of carboxylate anions. Amongst them, sugar-based esters are an attractive class of amphiphilic compounds which have been investigated for their properties as biosurfactants, emulsifying agents and stabilizers in the food and cosmetic industries.<sup>[2,7,8]</sup> However, the esterification reaction needs to be catalyzed and generally mineral acids are used, resulting in pollution and corrosion problems. Transesterification can be catalyzed by acids, bases or enzymes, but the use of soluble catalysts generates the same environmental problems in the scale up. An eco-friendly green approach is the use of heterogeneous catalysts as it allows the recovery of the catalyst and generally diminishes the amount of waste. For example, sorbitol fatty acid esters have been prepared in a two-step cascade reaction using heteropoly acids (HPA) catalysts.<sup>[8]</sup> Unfortunately, these catalysts have strong Brønsted acidity and are not compatible with protecting groups labile in acidic conditions and favor in this case the formation of anhydridized sorbitol esters.

Some of us have reported a rapid access of esterified and/or glycosylated derivatives of D-glucuronic acid from its 6,1-lactone under microwave irradiation.<sup>[9]</sup> The products were formed rapidly and the regioselectivity differs from that obtained in classical heating.<sup>[10]</sup> Particularly, we observed a chemoselectivity in favor of esterified compounds when the reactions were catalyzed by FeCl<sub>3</sub>, while SnCl<sub>4</sub> led to esterified and glycosylated products. The high reactivity and versatility of this 6,1 lactone allowed its rapid conversion to a variety of glucuronamides.<sup>[11]</sup> Simultaneously to this study, the synergy of microwaves and heterogeneous acid catalysts, on the reaction of D-glucuronic acid and alcohols has been reported.<sup>[12]</sup> Sulfuric acid and a Keggin type heteropolyacid (H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>) were impregnated on silica or siliceous MCM-41 and proved to catalyzed the formation of alkyl D-glucofuranosidurono-6,3-lactone derivatives. Depending on the solvent used, the deactivation of the catalysts was significant.

Polyoxometalates (POMs) have been the subject of intense research since the beginning of the 20th century.<sup>[13]</sup> Catalysis by these clusters of early transition metals in high oxidation states (W<sup>VI</sup>, Mo<sup>VI</sup>, V<sup>V</sup>) and oxo ligands – has been greatly expanding these last years.<sup>[14]</sup> As already mentioned above, protonated POMs (heteropolyacids, HPA) are often used as acid catalysts, including for solvent-free and multicomponent reactions.<sup>[15]</sup> We have introduced Lewis acidic POMs that have opened new options for chemists.<sup>[16]</sup> Lewis acidity was introduced *via* the incorporation of Lewis acidic

cations into lacunary Dawson type phosphotungstic structures (Figure 1), which allowed modulation of the catalytic activities.<sup>[17]</sup>

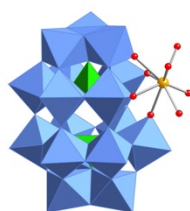


Figure 1. Dawson-type  $[\alpha_1\text{-M}(\text{H}_2\text{O})_4\text{P}_2\text{W}_{17}\text{O}_{61}]^{n-}$  polyanions

Herein, we report on the chemoselective esterification of GlcA 6,1-lactone **1** using  $[\alpha_1\text{-M}(\text{H}_2\text{O})_4\text{P}_2\text{W}_{17}\text{O}_{61}]^{n-}$  ( $\text{M} = \text{Yb}^{\text{III}}$ ,  $n = 7$ ;  $\text{Hf}^{\text{IV}}$  and  $\text{Zr}^{\text{IV}}$ ,  $n = 6$ ) Dawson-type POMs as reusable catalysts under microwave irradiation.

We first studied the reaction of the 2,3,4-tri-*O*-acetyl-D-glucopyranurono-6,1-lactone **1** with methanol in the presence of different Lewis acidic POMs as catalysts (Scheme 1, table 1). Interestingly the chemoselectivity was in favor of the formation of the methyl ester function leading to the compound **2a** with a free anomeric hydroxyl as the unique product. This scaffold can be used as an intermediate compound for the synthesis of phosphate derivatives<sup>[11]</sup> or molecules of interest.<sup>[3,4]</sup>



Scheme 1.

Table 1. Effects of POM catalyst on reaction of 6,1 lactone <b>1</b> with alcohols				
Entry	Catalyst (20 mol%)	MW conditions <sup>[a]</sup>	ROH [equiv]	Product; Yield [%]
1	POM-Yb (K)	50/65/10	MeOH (15)	<b>2a</b> ; 72
2	POM-Yb (TBA)	50/65/10	MeOH (15)	<b>2a</b> ; 72
3	POM-Hf	50/65/10	MeOH (15)	<b>2a</b> ; 81
4	POM-Zr	20/65/10	MeOH (15)	<b>2a</b> ; 80
5	POM-Zr	20/65/10	MeOH (150)	<b>2a</b> ; 94
6	FeCl <sub>3</sub>	3/65/10	MeOH (15)	<b>2a</b> ; 56
7	Yb(OTf) <sub>3</sub>	20/65/10	MeOH (15)	<b>2a</b> ; 60
8	POM-Zr	26/115/10	BuOH (15)	<b>2b</b> ; 35
9	POM-Zr	25/115/30	BuOH (15)	<b>2b</b> ; 67
10	FeCl <sub>3</sub>	25/115/30	BuOH (15)	/ <sup>b</sup>
11	Yb(OTf) <sub>3</sub>	25/115/30	BuOH (15)	/ <sup>b</sup>
12	POM-Zr	15/115/30	C <sub>8</sub> H <sub>17</sub> OH (15)	<b>2c</b> ; 56

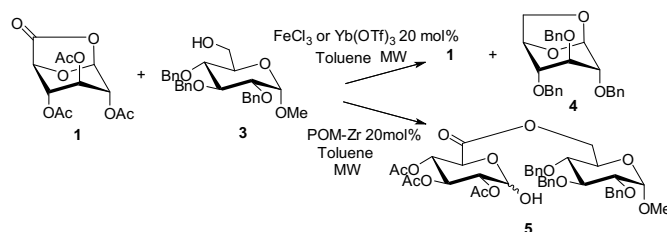
[a] Power (Watts)/Temperature (°C)/Time (min). [b] Only random deacetylation associated with glycosylation of **1** occurred.

The reaction was catalyzed by the ytterbium complex  $[\alpha\text{-Yb}(\text{H}_2\text{O})_4\text{P}_2\text{W}_{17}\text{O}_{61}]^{7-}$  (POM-Yb) associated with potassium or TBA (tetrabutylammonium) counterions (Table 1, entries 1, 2). In these conditions, the expected methyl glucuronate **2a** was isolated in 72% yield in less than 10 minutes. The use of catalysts with a higher Lewis acidic character ( $\text{TBA}_5\text{K}[\alpha\text{-Hf}(\text{H}_2\text{O})_4\text{P}_2\text{W}_{17}\text{O}_{61}]$  [POM-Hf] or  $\text{TBA}_5\text{K}[\alpha\text{-Zr}(\text{H}_2\text{O})_4\text{P}_2\text{W}_{17}\text{O}_{61}]$ , [POM-Zr]) increased the efficiency of the reaction, giving **2a** in good yield after 10 min (Table 1, entries 3, 4). We also noticed an effect of the amount of nucleophile. Indeed, degradation (dark products) were observed when only 5 eq of MeOH were used, whereas a larger excess allowed the isolation of **2a** in 94% yield (Table 1, entry 5). We compared the activity of these Lewis acidic POMs with more common Lewis catalysts such as  $\text{FeCl}_3$  and  $\text{Yb}(\text{OTf})_3$ . Both allowed the conversion of **1** into the expected product **2a** in slightly lower yields (Table 1, entries 6, 7). On the other hand, traditional Brønsted acidic POMs such as  $\text{H}_4\text{SiW}_{12}\text{O}_{40}$  and  $\text{H}_3\text{PW}_{12}\text{O}_{40}$  only catalyzed degradation of **1** in these conditions.

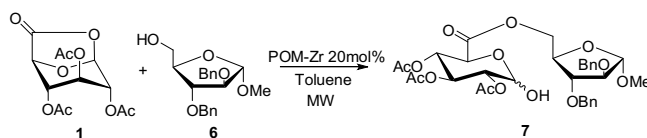
Next, owing to the specific solubilities of POMs, the recyclability of our catalysts in these reaction conditions was evaluated. After precipitation with diethylether, the POM-Hf catalyst (Table 1, entry 3) could be recovered by filtration (in 82 % yield) or centrifugation (in 93% yield). No traces of catalyst could be observed by  $^1\text{H}$  or  $^{31}\text{P}$  NMR in the filtrate. Besides,  $\text{Yb}^{3+}$  is paramagnetic and the leached material would influence the NMR spectra of the organic phase. Since no paramagnetic shift or line broadening was observed, it was deduced that no free  $\text{Yb}^{3+}$  remains in solution. We then reused the catalyst in the same conditions to afford **2a** in 81 %, 75%, 73% and 68% for the first, the second, third, and fourth cycles respectively. We feel that this decrease could be the result of a slight degradation of our catalyst. No change was observed by  $^{31}\text{P}$  NMR or IR after the two first cycles. On the other hand, a  $^{31}\text{P}$  NMR analysis of the POM-Hf catalyst after the fourth recycling presented some new phosphorus signals, confirming the slow degradation of the polyoxotungstate in these conditions. The POM-Zr (recovered in 93% yield by centrifugation) was used twice with no significative loss of activity nor degradation observable by  $^{31}\text{P}$  NMR or IR (Table 1, entry 4).

The reaction with alcohols of different alkyl chain length was examined next. Treated with *n*-butanol, the lactone **1** gave the corresponding glucopyranuronate **2b** in 35% in 10 minutes at 115°C (Table 1, entry 8). The yield reached 67% when reaction was carried out for 30 minutes (entry 9). At the same temperature, the use of  $\text{FeCl}_3$  and  $\text{Yb}(\text{OTf})_3$  associated to *n*-butanol resulted in unselective deacetylation and glycosylation at the anomeric position (Table 1, entries 9-11). The octyl derivative **2c** was isolated in only 56% even after 30 min. As we have observed previously, yields of alkyl glucopyranuronates decreased when the chain length increased.<sup>[9]</sup>

More interestingly, these catalysts were tested for the coupling of **1** with two representative sugar derivatives as nucleophiles (Scheme 2 and 3, Table 2). These reactions failed when traditional Lewis acidic catalysts were used. For example, using  $\text{FeCl}_3$  or  $\text{Yb}(\text{OTf})_3$ , methyl 2,3,4-tri-*O*-benzyl-D-glucopyranoside **3** did not react with the lactone **1** but cyclized intramolecularly into the corresponding levoglucosan **4**<sup>[18]</sup> (Scheme 2 and table 2, entries 1, 2)).



Scheme 2.



Scheme 3.

Table 2. Reaction of 6,1 lactone <b>1</b> with sugar acceptor.				
Entry	Catalyst (20 mol%)	MW conditions <sup>[a]</sup>	SuOH [1.2 equiv] <sup>[b]</sup>	Product; Yield [%]
1	FeCl <sub>3</sub>	24/85/30	<b>3</b>	<b>4</b> ; 63
2	Yb(OTf) <sub>3</sub>	35/110/30	<b>3</b>	<b>4</b> ; 24
3	POM-Zr	38/110/30	<b>3</b>	<b>5</b> ; 46
4	POM-Zr	23/110/30	<b>6</b>	<b>7</b> ; 66

[a] Power (Watts)/Temperature (°C)/Time (min) [b] All reactions were carried out in toluene (0.4 mL for 50 mg of 6,1-lactone **1**).

In our study, we demonstrated that the used of only 1.2 equiv of sugar derivatives **3** or **6** in association with POM-Zr (20 mol%) in minimum amount of toluene allowed the conversion of compound **1** into the corresponding pseudo-disaccharides **5** and **7** in 46% and 66% yield, respectively. Compounds **5** and **7** are the only products formed, the remainder being starting material. Beyond 30 minutes, a low deacetylation is observed. Again, the recyclability of the catalyst was studied. Compound **7** was obtained in 66, 61 and 56% yield, after the first, second and third run respectively (Table 2, entry 4). This is to our knowledge, the first recoverable selective Lewis acid catalyst for this reaction. Such compounds are valuable products since, aldonic esters are intermediates in redox glycosidation for the synthesis of 1→6 linked disaccharides *via* a thionation and reductive desulfurization.<sup>[19]</sup>

In conclusion, we reported the use of Lewis acidic POMs as mild and selective catalysts for the transesterification of the 2,3,4-tri-*O*-acetyl-D-glucopyranurono-6,1-lactone under microwave irradiation. While reactions carried out with glucuronic acid gave esterified-glucosylated derivatives, its 6,1-lactone catalyzed with POMs provided only esterified compounds with free anomeric hydroxyl as key intermediates for the synthesis of more complex molecules. These catalysts allowed chemoselective formation of pseudo-disaccharides from easily available precursors. This permitted the expeditious assembly of promising building blocks from precursors obtained from the biomass, with easy recycling of the catalyst. Further work will focus on other targets using renewable feedstocks.

## Experimental Section

General information: methanol (HPLC grade), butan-1-ol (anhydrous over molecular sieves 4Å), octan-1-ol (anhydrous), dichloromethane (reactant grade), toluene (anhydrous over molecular sieves 4Å) were purchased from Acros or Sigma-Aldrich. Thin-layer chromatography (TLC) was performed on silica gel 60 F254 (Merck) alumina rolls with visualization by UV light (254 nm) and/or charring with a vanillin-H<sub>2</sub>SO<sub>4</sub> reagent. Preparative column chromatography was performed using 230–400 mesh Merck silica gel (purchased from Aldrich). <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker 300 WB spectrometer at 300 and 75 MHz, respectively. High resolution electrospray experiments were performed on a Waters-Micromass Q-TOF Ultima Global hybrid quadrupole time-of-flight instrument, equipped with an electrospray (Z-spray) ion source (Waters-Micromass, Manchester, UK). Microwave irradiation was performed in a CEM Discover® System.

Typical procedure for the transesterification catalyzed by POM: To 6,1-glucuro-lactone **1** (50 mg, 165 μmol) and POM (0.2 eq.) was added the alcohol or sugar nucleophile (15 or 1.2 equiv) in a tube equipped with a stirring magnetic bar under argon atmosphere. The mixture was irradiated at 65 or 110°C during 10 min or 30 min. Diethylether (20 mL) was added to the reaction mixture to precipitate POM catalyst, which was removed by filtration. Concentration of the filtrate under reduced pressure followed by flash chromatography (silica gel 7g, ethyl acetate/cyclohexane, 3:7) afforded the corresponding glucopyranuronate ester as a mixture of α,β anomers:

### 1-Methyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranosyl 2,3,4-tri-*O*-acetyl-D-glucopyranuronate **5**

Colorless oil. R<sub>f</sub>=0.32 (AcOEt/cyclohexane 1:1); α anomer <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 25°C): δ=7.40-7.21 (m, 15H, H aromatics), 5.53 (dd, <sup>3</sup>J(H<sub>2</sub>,H<sub>3</sub>)=9.8 Hz, <sup>3</sup>J(H<sub>3</sub>,H<sub>4</sub>)=9.4 Hz, 1H; H<sub>3</sub>GlcA), 5.47 (d, <sup>3</sup>J(H<sub>1</sub>,H<sub>2</sub>)=3.5 Hz, 1H; H<sub>1</sub>GlcA), 5.18 (dd, <sup>3</sup>J(H<sub>3</sub>,H<sub>4</sub>)=9.4 Hz, <sup>3</sup>J(H<sub>4</sub>,H<sub>5</sub>)=10 Hz, 1H; H<sub>4</sub>GlcA), 4.97 (d, <sup>3</sup>J(H,H)=10.8 Hz, 1H; OCH<sub>2</sub>Ph), 4.89 (dd, <sup>3</sup>J(H<sub>1</sub>,H<sub>2</sub>)=3.5 Hz, <sup>3</sup>J(H<sub>2</sub>,H<sub>3</sub>)=9.8 Hz, 1H; H<sub>2</sub>GlcA), 4.85 (d, <sup>3</sup>J(H,H)=11.2 Hz, 1H; OCH<sub>2</sub>Ph), 4.80 (d, <sup>3</sup>J(H,H)=10.8 Hz, 1H; OCH<sub>2</sub>Ph), 4.79 (d, <sup>3</sup>J(H,H)=12 Hz, 1H; OCH<sub>2</sub>Ph), 4.66 (d, <sup>3</sup>J(H,H)=12 Hz, 1H; OCH<sub>2</sub>Ph), 4.56 (d, <sup>3</sup>J(H<sub>4</sub>,H<sub>5</sub>)=10 Hz, 1H; H<sub>5</sub>GlcA), 4.52 (d, <sup>3</sup>J(H,H)=11.2 Hz, 1H; OCH<sub>2</sub>Ph), 4.52 (d, <sup>3</sup>J(H<sub>1</sub>,H<sub>2</sub>)=3.6 Hz, H<sub>1</sub>Glc), 4.40 (dd, <sup>3</sup>J(H<sub>5</sub>,H<sub>6</sub>)=2.3 Hz, <sup>3</sup>J(H<sub>6</sub>,H<sub>6</sub>)=11.8 Hz, 1H; H<sub>6</sub>Glc), 4.20 (dd, <sup>3</sup>J(H<sub>5</sub>,H<sub>6</sub>)=5.6 Hz, <sup>3</sup>J(H<sub>6</sub>,H<sub>6</sub>)=11.8 Hz, 1H; H<sub>6</sub>Glc), 3.99 (t, <sup>3</sup>J(H<sub>2</sub>,H<sub>3</sub>)=<sup>3</sup>J(H<sub>3</sub>,H<sub>4</sub>)=9.3 Hz, 1H; H<sub>3</sub>Glc), 3.81 (ddd, <sup>3</sup>J(H<sub>4</sub>,H<sub>5</sub>)=10 Hz, <sup>3</sup>J(H<sub>5</sub>,H<sub>6</sub>)=2.3 Hz, <sup>3</sup>J(H<sub>5</sub>,H<sub>6</sub>)=5.6 Hz, 1H; H<sub>5</sub>Glc), 3.54 (dd, <sup>3</sup>J(H<sub>1</sub>,H<sub>2</sub>)=3.6 Hz, <sup>3</sup>J(H<sub>2</sub>,H<sub>3</sub>)=6.9 Hz, 1H; H<sub>2</sub>Glc), 3.38 (dd, <sup>3</sup>J(H<sub>3</sub>,H<sub>4</sub>)=9.4 Hz, <sup>3</sup>J(H<sub>4</sub>,H<sub>5</sub>)=10 Hz, 1H; H<sub>4</sub>Glc), 3.36 (s, 3H; OCH<sub>3</sub>), 2.07 (s, 3H; COCH<sub>3</sub>), 2.02 (s, 3H; COCH<sub>3</sub>), 1.90 ppm (s, 3H; COCH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, 25°C): δ=170.2, 169.5 (3C; COCH<sub>3</sub>), 168.0 (C<sub>6</sub>GlcA), 138.5, 137.9, 137.8 (3C; C<sub>q</sub> aromatics), 128.5, 128.3, 128.1, 128.0, 127.8, 127.7 (15C; CH aromatics), 97.9 (C<sub>1</sub>Glc), 90.2 (C<sub>1</sub>GlcA), 81.9 (C<sub>3</sub>Glc), 79.8 (C<sub>2</sub>Glc), 77.5 (C<sub>4</sub>Glc), 75.8, 74.9, 73.7 (3C; OCH<sub>2</sub>Ph), 70.7 (C<sub>2</sub>GlcA), 69.6 (C<sub>4</sub>GlcA), 69.4 (C<sub>3</sub>GlcA), 68.4 (C<sub>5</sub>Glc), 68.0 (C<sub>5</sub>GlcA), 64.8 (C<sub>6</sub>Glc), 55.2 (OCH<sub>3</sub>), 20.7, 20.5 ppm (3C; COCH<sub>3</sub>). β anomer (selected data) <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 25°C): δ=5.28-5.23 (m, 2H; H<sub>3</sub>GlcA, H<sub>4</sub>GlcA), 4.68 (d, <sup>3</sup>J(H,H)=10.8 Hz, 1H; OCH<sub>2</sub>Ph), 4.11-4.07 ppm (m, 1H; H<sub>5</sub>Glc); <sup>13</sup>C NMR (75

MHz, CDCl<sub>3</sub>, 25°C): δ=170.4 (COCH<sub>3</sub>), 169.3 (COCH<sub>3</sub>), 167.0 (C6GlcA), 73.5 (OCH<sub>2</sub>Ph), 72.7 (2C; C2GlcA, C5GlcA), 71.8 (C3GlcA), 69.3 (C4GlcA), 64.7 (C6Glc), 55.3 ppm (OCH<sub>3</sub>); HRMS (TOF MS ES+): *m/z* calcd for C<sub>40</sub>H<sub>46</sub>O<sub>15</sub>Na: 789.2734, found: 789.2723.

#### 1-Methyl-2,3-di-O-benzyl-α-D-arabinofuranosyl 2,3,4-tri-O-acetyl-β-D-glucopyranuronate 7

Colorless oil. R<sub>f</sub>=0.40 (AcOEt/cyclohexane 1:1); α anomer <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 25°C): δ=7.40-7.23 (m, 10H, H aromatics), 5.59 (broad t, <sup>3</sup>J(H<sub>2</sub>,H<sub>3</sub>)=10 Hz, <sup>3</sup>J(H<sub>3</sub>,H<sub>4</sub>)=9.5 Hz, 1H; H<sub>3</sub>GlcA), 5.46 (d, <sup>3</sup>J(H<sub>1</sub>,H<sub>2</sub>)=3.5 Hz, 1H; H<sub>1</sub>GlcA), 5.16 (dd, <sup>3</sup>J(H<sub>3</sub>,H<sub>4</sub>)=9.5 Hz, <sup>3</sup>J(H<sub>4</sub>,H<sub>5</sub>)=10 Hz, 1H; H<sub>4</sub>GlcA), 4.91 (broad s, 1H; H<sub>1</sub>Ara), 4.87 (dd, <sup>3</sup>J(H<sub>1</sub>,H<sub>2</sub>)=3.5 Hz, <sup>3</sup>J(H<sub>2</sub>,H<sub>3</sub>)=10 Hz, 1H; H<sub>2</sub>GlcA), 4.57 (d, <sup>3</sup>J(H<sub>4</sub>,H<sub>5</sub>)=10 Hz, 1H; H<sub>5</sub>GlcA), 4.56 (d, <sup>3</sup>J(H,H)=11.9 Hz, 1H; OCH<sub>2</sub>Ph), 4.54 (d, <sup>3</sup>J(H,H)=11.8 Hz, 1H; OCH<sub>2</sub>Ph), 4.47 (d, <sup>3</sup>J(H,H)=11.9 Hz, 1H; OCH<sub>2</sub>Ph), 4.46 (d, <sup>3</sup>J(H,H)=11.8 Hz, 1H; OCH<sub>2</sub>Ph), 4.38 (dd, <sup>3</sup>J(H<sub>4</sub>,H<sub>5</sub>)=3.3 Hz, <sup>3</sup>J(H<sub>5</sub>,H<sub>5'</sub>)=11.6 Hz, 1H; H<sub>5</sub>Ara), 4.20 (td, <sup>3</sup>J(H<sub>3</sub>,H<sub>4</sub>)=<sup>3</sup>J(H<sub>4</sub>,H<sub>5</sub>)=6.6 Hz, <sup>3</sup>J(H<sub>4</sub>,H<sub>5</sub>)=3.3 Hz, 1H; H<sub>4</sub>Ara), 4.07 (dd, <sup>3</sup>J(H<sub>4</sub>,H<sub>5</sub>)=6.6 Hz, <sup>3</sup>J(H<sub>5</sub>,H<sub>5'</sub>)=11.6 Hz, 1H; H<sub>5</sub>'Ara), 3.98 (dd, <sup>3</sup>J(H<sub>1</sub>,H<sub>2</sub>)=1 Hz, <sup>3</sup>J(H<sub>2</sub>,H<sub>3</sub>)=2.8 Hz, 1H; H<sub>2</sub>Ara), 3.76 (dd, <sup>3</sup>J(H<sub>2</sub>,H<sub>3</sub>)=2.8 Hz, <sup>3</sup>J(H<sub>3</sub>,H<sub>4</sub>)=6.6 Hz, 1H; H<sub>3</sub>Ara), 3.36 (s, 3H; OCH<sub>3</sub>), 2.06 (s, 3H; COCH<sub>3</sub>), 2.01 (s, 3H; COCH<sub>3</sub>), 2.00 ppm (s, 3H; COCH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, 25°C): δ=170.2, 169.8 (3C; COCH<sub>3</sub>), 168.0 (C6GlcA), 137.5, 137.2 (2C; Cq aromatics), 128.6, 128.2, 128.1, 127.9 (8C; CH aromatics), 107.5 (C1Ara), 90.2 (C1GlcA), 87.7 (C2Ara), 83.8 (C3Ara), 79.1 (C4Ara), 72.4, 72.2 (2C; OCH<sub>2</sub>Ph), 70.7 (C2GlcA), 69.5 (C4GlcA), 69.3 (C3GlcA), 68.0 (C5GlcA), 65.8 (C5Ara), 55.2 (OCH<sub>3</sub>), 20.8, 20.6 ppm (3C; COCH<sub>3</sub>). β anomer (selected data) <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, 25°C): δ=5.27-5.22 (m, 2H; H<sub>3</sub>GlcA, H<sub>4</sub>GlcA), 4.68 (d, <sup>3</sup>J(H<sub>1</sub>,H<sub>2</sub>)=6.9 Hz, 1H; H<sub>1</sub>GlcA), 3.79 ppm (dd, <sup>3</sup>J(H<sub>2</sub>,H<sub>3</sub>)=2.3 Hz, <sup>3</sup>J(H<sub>3</sub>,H<sub>4</sub>)=6.1 Hz, 1H; H<sub>3</sub>Ara); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, 25°C): δ=167.5 (C6GlcA), 95.4 (C1GlcA), 83.7 (C3Ara), 79.3 (C4Ara), 73.0 (C2GlcA), 72.3 (C5GlcA), 71.7 (C3GlcA), 69.2 (C4GlcA), 65.5 ppm (C5Ara); HRMS (TOF MS ES+): *m/z* calcd for C<sub>32</sub>H<sub>38</sub>O<sub>14</sub>Na: 669.2159, found: 669.2155.

## Acknowledgements

The authors acknowledge the 'Conseil Régional de Picardie', CNRS, IUF, the « Ministère de l'Education Nationale, de l'Enseignement Supérieur et de la Recherche », and ANR (grant JC05\_41806 to E.L., ST, and B.H.) for financial support of this work.

**Keywords:** Glucuronic acid · Esterification · Polyoxometalates · Microwave · Lewis acids.

- [1] H. Razafindralambo, C. Blecker, S. Mezdour, C. Deroanne, J.M. Crowet, R. Brasseur, L. Lins, M. Paquot, Michel J. Phys.Chem. B **2009**, *113*, 8872-8877
- [2] a) J. Guilbot, T. Benvegnu, N. Legros, D. Plusquellec, *Langmuir* **2001**, *17*, 613-618. b) M. Berchel, L. Lemiègre, J. Jęflic, T. Benvegnu, *Tetrahedron Lett.* **2008**, *49*, 4690-4692. c) M. Berchel, L. Lemiègre, S. Trépout, O. Lambert, J. Jęflic, T. Benvegnu, *Tetrahedron Lett.* **2008**, *49*, 7419-7422.
- [3] a) R.W.M. Aben, J.W. Scheeren, J.J. Cornelissen, M. Lamberuts, D. De Vos, H.J. Haisma, EP 2098533, **2009**. b) P. Wang, Z. Zhang, B. Yu, *J. Org. Chem.* **2005**, *70*, 8884-8889. c) J.H.P. Thenot, P. Espie, J. Allen, H. Depoortere, WO 9961457, **1999**. d) F. Scheinmann, S. Joel, A.V. Stachulski, US 5977326, **1999**. e) J.F. Rossignol, A.V. Stachulski, *J. Chem. Res., Synopses* **1999**, *1*, 44-45.
- [4] a) N. Al-Maharik, N.P. Botting, *Eur. J. Org. Chem.* **2008**, *33*, 5622-5629. b) J.R. Harding, C.D. King, J.A. Perrie, D. Sinnott, A.V. Stachulski, *Org. Biomol. Chem.* **2005**, *3*, 1501-1507. c) L.X. Wang, A. Heredia, H. Song, Z. Zhang, B. Yu, C. Davis, R. Redfield, *J. Pharm. Sci.* **2004**, *93*, 2448-2457. d) P.M. O'Neill, F. Scheinmann, A.V. Stachulski, J.L. Maggs, B.K. Park, *J. Med. Chem.* **2001**, *44*, 1467-1470. e) I. Rukhman, L. Yudovich, G. Nisnevich, A.L. Gutman, *Tetrahedron* **2001**, *57*, 1083-1092.
- [5] a) M. Thomas, J. Clarhaut, I. Tranoy-Opalinski, J.P. Gesson, J. Roche, S. Papot, *Bioorg. Med. Chem.* **2008**, *16*, 8109-8116. b) R.G.G. Leenders, E.W.P. Damen, E.J.A. Bijsterveld, H.P.J. Scheeren, P.H.J. Houba, I.H. Van der Meulen-Muileman, E. Boven, H.J. Haisma, *Bioorg. Med. Chem.* **1999**, *7*, 1597-1610. c) R.G.G. Leenders, K.A.A. Gerrits, R. Ruijtenbeek, H.W. Scheeren, H.J. Haisma, E. Boven, *Tetrahedron Lett.* **1995**, *36*, 1701-4.
- [6] a) C. Gauthier, J. Legault, S. Rondeau, A. Pichette, *Tetrahedron Lett.* **2009**, *50*, 988-991. b) L.F. Tietze, H.J. Schuster, K. Schmuck, I. Schubert, F. Alves, *Bioorg. Med. Chem.* **2008**, *16*, 6312-6318.
- [7] a) D.L. Brown US 2010125051, **2010**. b) M. Fanun *J. Disp. Sci. Technol.* **2009**, *30*, 399-405. c) H. Razafindralambo, C. Blecker, S. Mezdour, C. Deroanne, J.M. Crowet, R. Brasseur, L. Lins, M. Paquot, Michel J. Phys. Chem. B **2009**, *113*, 8872-8877. d) V.B. Patravale, P.D. Dandekar, IN 2006MU01945, **2008**. e) M.K. Taylor, PCT Int. **2006**, WO 2006076222; f) C. Blecker, S. Piccicuto, G. Lognay, C. Deroanne, M. Marlier, M. Paquot, *J. Colloid Int. Sc.* **2002**, *247*, 424-428. g) C. Stubenrauch, *Curr. Opin. Colloid Interface Sci.* **2001**, *6*, 160-170.
- [8] A. Corma, S.B.A. Hamid, S. Iborra, A. Velty, *ChemSusChem* **2008**, *1* 85-90.
- [9] S. Rat, D. Mathiron, P. Michaud, J. Kovensky, A. Wadouachi, *Tetrahedron*, **2007**, *63*, 12424-12428.
- [10] a) M. Polakova, N. Pitt, M. Tosin, P.V. Murphy, *Angew. Chem. Int. Ed.* **2004**, *43*, 2518-2521. b) C. O'Brien, M. Polakova, N. Pitt, M. Tosin, P.V. Murphy, *Chem. Eur. J.* **2007**, *13*, 902-909.
- [11] M. Bosco, S. Rat, J. Kovensky, A. Wadouachi, *Tetrahedron Lett.* **2010**, *51*, 2553-2556.
- [12] A. Richel, P. Laurent, B. Wathelet, J.P. Wathelet, M. Paquot, *Tetrahedron Lett.* **2010**, *51*, 1356-1360.
- [13] a) Polyoxo anions: Synthesis and Structure": M. T. Pope, in *Comprehensive Coordination Chemistry II, Vol. 4* (Ed.: A. G. Wedd), Elsevier, Oxford, **2004**, pp. 635-678. b) "Polyoxometalates: Reactivity": C. L. Hill, in *Comprehensive Coordination Chemistry II, Vol. 4* (Ed.: A. G. Wedd), Elsevier, Oxford, **2004**, pp. 679-759. c) L. E. Briand, G. T. Baronetti, H. J. Thomas, *Appl. Catal., A* **2003**, *256*, 37-50. d) M.N. Timofeeva *Appl. Catal., A* **2003**, *256*, 19-35.
- [14] a) M. Misono, *Catal. Today* **2005**, *100*, 95-100. b) "Applications of Polyoxometalates in Homogeneous Catalysis": R. Neumann in *Polyoxometalate Molecular Science*, Vol. 98; J. J. Borrás-Almenar, E. Coronado, A. Müller, M. T. Pope, Eds.; Kluwer, Dordrecht, **2003**, p. 327-349. c) "Heterogeneous Catalysis by Heteropoly Compounds", I. V. Kozhevnikov, *ibid.*, p. 351-380. d) X. Fang, C. L. Hill *Angew. Chem. Int. Ed.* **2007**, *46*, 3877-3880. e) J. Geboers, S. Van de Vyver, K. Carpentier, K. de Blochouse, P. Jacobs, B. Sels, *Chem. Commun.*, **2010**, **46**, 3577-3579.

- [15] a) M. Misono *Chem. Commun.* **2001**, 1141-1152. b) N. Azizi, L. Torkiyan, M. R. Saidi *Org. Lett.* **2006**, *8*, 2079-2082. L. Nagarapu, S. Apuri, S. Kantevari *J. Mol. Catal. A: Chem.* **2007**, *266*, 104-108. c) Y. Leng, J. Wang, D. Zhu, Y. Wu, P. Zhao, J. Mol. Catal. A : Chem. 2009, *313*, 1-6
- [16] C. Boglio, G. Lenoble, C. Duhayon, B. Hasenknopf, R. Thouvenot, C. Zhang, R. C. Howell, B. P. Burton-Pye, L. C. Francesconi, E. Lacôte, S. Thorimbert, M. Malacria, C. Afonso, J.-C. Tabet, *Inorg. Chem.* **2006**, *45*, 1389-1398.
- [17] a) C. Boglio, G. Lemièrre, B. Hasenknopf, S. Thorimbert, E. Lacôte, M. Malacria, *Angew. Chem.* **2006**, *118*, 3402-3405; *Angew. Chem. Int. Ed.* **2006**, *45*, 3324-3327; b) C. Boglio, K. Micoine, P. Rémy, B. Hasenknopf, S. Thorimbert, E. Lacôte, M. Malacria, C. Afonso, J.-C. Tabet, *Chem. Eur. J.* **2007**, *13*, 5426-5432; c) Y. Kikukawa, S. Yamaguchi, Y. Nakagawa, K. Uehara, S. Uchida, K. Yamaguchi, N. Mizuno, *J. Am. Chem. Soc.* **2008**, *130*, 15872-15878; d) Y. Kikukawa, S. Yamaguchi, K. Tsuchida, Y. Nakagawa, K. Uehara, K. Yamaguchi, N. Mizuno, *J. Am. Chem. Soc.* **2008**, *130*, 5472-5478; e) X. Zhang, J. Li, Y. Chen, J. Wang, L. Feng, X. Wang, F. Cao *Energy Fuels* **2009**, *23*, 4640-4646; f) J. Li; X. Zhang;; W. Zhu; F. Cao *ChemSusChem* **2009**, *2*, 177-183; g) N. Dupré, P. Rémy, K. Micoine, C. Boglio, S. Thorimbert, E. Lacôte, B. Hasenknopf, M. Malacria *Chem. Eur. J.* **2010**, *16*, 7256-7264.
- [18] S. J. Sondheimer, R. Eby, C. Schuerch, *Carbohydr. Res.* **1978**, *60*, 187-192.
- [19] A.G.M. Barrett, A.C. Lee, *J. Org. Chem.* **1992**, *57*, 2818-2825.
-