Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron 63 (2007) 12424–12428
Tetrahedron

Efficient glycosydation and/or esterification of D-glucuronic acid and its 6,1-lactone under solvent-free microwave irradiation

Stéphanie Rat,[a] David Mathiron,[a] Philippe Michaud,[b] José Kovensky[a] and Anne Wadouachi[a,*]

[a]*Laboratoire des Glucides UMR CNRS 6219, Université de Picardie Jules Verne, 33 Rue Saint-Leu, F-80039 Amiens, France*
[b]*Laboratoire de Génie chimique Université de Blaise Pascal-Polytech, 24 rue des Landais, F-63174 Aubière, France*

Received 2 July 2007; revised 5 September 2007; accepted 17 September 2007
Available online 23 September 2007

Abstract—2,3,4-Tri-*O*-acetyl-D-glucurono-6,1-lactone was obtained 'one-pot' from D-glucuronic acid. The lactone opening with different alcohols in the presence of a variety of catalysts was studied. All reactions were performed under microwave irradiation in solvent-free conditions.

1. Introduction

Recent advances in carbohydrate chemistry are essentially connected to the synthesis of complex targets of high added value and specific biological activity and are based on the development of subtle strategies to access selectively to these molecules.

Selectivity is a crucial objective in organic synthesis and is classically achieved by applying kinetic vs thermodynamic control, by using selective catalysts, or by selecting appropriate reaction conditions: solvent, temperature, and time.

In recent decades, microwaves (MW) have found application in various organic reactions, including alkylations, nucleophilic substitutions, condensations, cyclo-additions, and reactions introducing or cleaving protecting groups.[1–5]

Compared to conventional methods, reactions under microwaves usually show shorter reaction times, higher stereoselectivity, and increased yields.[6] Solvent-free methods are specially adapted to green chemistry principles.[7] When coupled to microwave irradiation, they result in very efficient and clean procedures with noticeable improvements over classical methods.

Glycosides of D-glucuronic acid (GlcA) are ubiquitous components of oligo- and polysaccharides of biological significance. Glucuronidation is a well-known drug-metabolizing reaction and is generally regarded as a detoxification process involving drug–glucuronic acid adducts. Recently, the synthesis of glucuronyl prodrugs for application in Antibody Directed Enzyme-Prodrug Therapy (ADEPT) or in Prodrug Monotherapy (PMT) has been proposed for enhancing selective administration of anticancer drugs and has been the subject of intense investigations.[8]

We are interested in developing a rapid access to modified uronate derivatives. Herein we describe the one-pot lactonization of GlcA and the lactone opening with alcohols in the presence of a variety of catalysts under MW irradiation in solvent-free conditions.

2. Results and discussion

The CEM Discover MW allows to irradiate under two modes: either an assigned power with continuous measure of the resulting temperature by an IR captor or an assigned temperature with continuous adjustment of the irradiation power. We chose the second mode, in solvent-free conditions with assigned temperature to avoid degradation of sugars by browning reactions.

We first studied the reaction of GlcA with methanol in the presence of various catalyts (Fig. 1, Table 1).

As it was previously reported using classical methods,[9] the use of MW activation led to D-glucofuranosidurono-6,3-lactone **1a**[10] from which alkyl GlcA derivatives can be easily obtained. The use of promoters such as thionyl chloride and sulfuric acid gave compound **1a** in moderate yields; these drastic conditions also led to partial decomposition

Keywords: Glucuronic acid; Glycosidation; Esterification; Microwave irradiation.
* Corresponding author. Tel.: +33 3 22 82 75 27; fax: +33 3 22 82 75 60; e-mail: anne.wadouachi@u-picardie.fr

0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.09.043

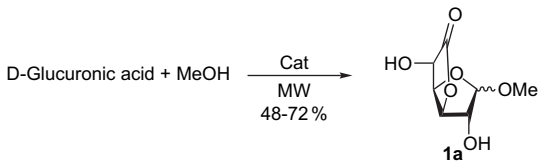


Figure 1.

Table 1. Effect of catalysts on convertion of GlcA into **1a**

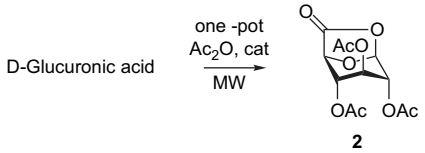
Catalyst (equiv)	MW conditions[a]	**1a** % Yield (α/β)
$SOCl_2$ (2 equiv)	60/70/10	48 (55/45)
H_2SO_4 (0.1 equiv)	10/60/10	56 (45/55)
$ZnCl_2$ (1 equiv)	80/85/10	39 (45/55)
p-TsOH (0.3 equiv)	20/70/10	72 (40/60)

[a] Power (Watts)/temperature (°C)/time (min).

of sugar. Surprisingly, a lower yield for the formation of **1a** was obtained with the use of promoter such as $ZnCl_2$, already described as an efficient catalyst.[11]

As shown in Table 1, the reaction time was the same (10 min) for all catalysts assayed. Best yield of **1a** was obtained with *p*-TsOH, a strong-acid, non-volatile solid, easy to manipulate and the most appropriate for solvent-free microwave synthesis.[12] The required microwave power was different for each promoter. When an irradiation power of 20 W was supplied to 6 equiv of methanol and 0.3 equiv of *p*-TsOH, compound **1a** was isolated in 72% yield.

An alternative route to GlcA derivatives is the 2,3,4-tri-*O*-acetyl-D-glucopyranosylurono-6,1-lactone **2**[13] that has been already prepared in two steps from GlcA in 65% overall yield.[14] We performed this reaction under microwave irradiation in the presence of a catalyst. In these conditions, GlcA was converted 'one-pot' into **2** (Scheme 1). Three catalysts were tested to define the most effective (Table 2).



Scheme 1.

The use of $ZnCl_2$ gave the 6,1-lactone **2** in a poor yield. $InCl_3$ has been described as catalyst for acylation of carbohydrate by MW irradiation, using a small quantity of acetonitrile.[15] In our conditions, catalysis with $InCl_3$ gave compound **2** in 85% yield. Finally, using iodine[16] as promoter, GlcA was converted in 10 min into **2** in 92% yield. This reaction has been scaled up to 10 g in same high yields.

Table 2. One-pot acetylation–lactonization of D-glucuronic acid

Catalyst (equiv)	MW conditions[a]	**2** % Yield
$ZnCl_2$ (1 equiv)	115/85/13	34
$InCl_3$ (0.1 equiv)	300/115/10	85
I_2 (0.3 equiv)	300/115/10	92

[a] Power (Watts)/temperature (°C)/time (min).

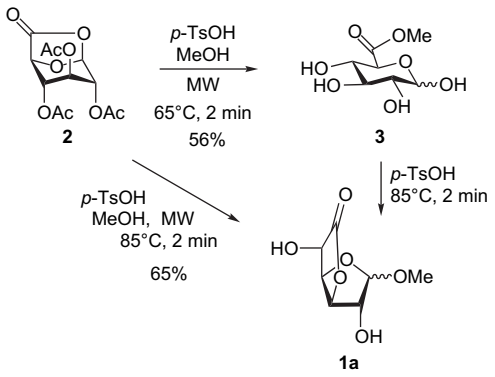
Table 3. Effect of catalysts on 6,1-lactone **2** with methanol

Catalyst (1 equiv)	MW conditions[a]	Products	% Yield (α/β)
$Yb(OTf)_3$	50/85/10	Mixture	—
$ZnCl_2$	110/95/10	**1a**	38 (60/40)
$BF_3 \cdot OEt_2$	20/70/5	**1a+4a**	41 (20/80), 59 (60/40)
p-TsOH[b]	110/85/5	**1a**	93 (30/70)
K10	50/85/10	—	—
KSF	50/85/10	**5a**	37 (55/45)
$SnCl_4$	15/70/2	**4a**	93 (80/20)
$FeCl_3$	40/60/2	**5a**	98 (75/25)

[a] Power (Watts)/temperature (°C)/time (min).
[b] Catalyst (0.3 equiv).

Reaction of 6,1-lactone **2** with methanol was then studied in the presence of different Lewis acids (Table 3). Metal triflate such as $Yb(OTf)_3$ was not effective and gave a complex mixture. Metal salt such as $ZnCl_2$ gave the D-glucofuranosidurono-6,3-lactone **1a** with a very moderate yield. The use of $BF_3 \cdot OEt_2$ led to a mixture of pyranose and furanose derivatives with simultaneous deacetylation.

p-TsOH catalyzed the transformation of **2** into the 6,3-lactone **1a** in a high yield (93%). We noted a selectivity in favor of β anomer. With this catalyst, simultaneous deacetylation occurred rapidly. Moreover, we observed that the chemoselectivity of the reaction is temperature dependent (Scheme 2).



Scheme 2.

Treated with methanol in the presence of a catalytic amount of *p*-TsOH at 65 °C, the lactone **2** gave in 2 min the methyl glucopyranuronate **3**[17] in 56% yield. When a higher temperature was reached (85 °C), methyl glucofuranosidurono-6,3-lactone **1a** was then isolated. We have confirmed that action of *p*-TsOH (2 min at 85 °C) on compound **3** led to **1a**.

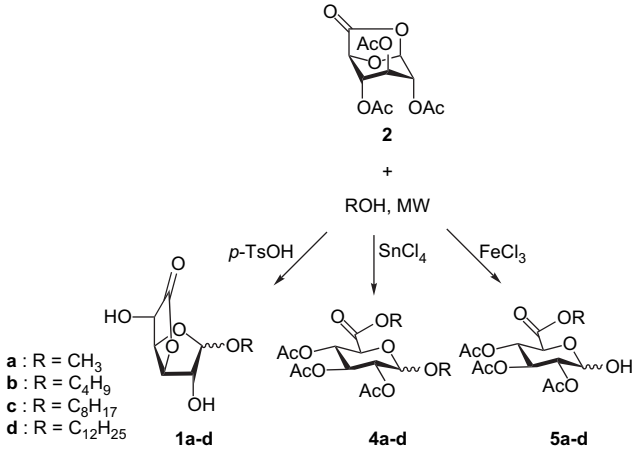
Montmorillonite clay–microwave combination has been already used as catalyst to achieve many organic transformations.[18] So we have tested two of them: K10 and KSF, the former gave no reaction, whereas the latter furnished only the esterified compound **5a**[19] with a poor yield (Table 3).

Murphy et al. have reported the glycosidation of the 6,1-lactone **2** with different acceptors in the presence of $SnCl_4$ at room temperature in CH_2Cl_2. The reaction time was 15 h and good yields were obtained with silyl ethers. Only the glycosidation reaction was observed, with no esterification of the carboxylic acid.[14,20] Under MW conditions, with the

same catalyst glycosidation and esterification reactions occurred in 5 min; compound **4a**[21] was obtained in 93% yield with a selectivity in favor of α anomer (Table 3).

On the other hand, the use of $FeCl_3$ as promoter led to methyl ester **5a** in 98% yield and in short time (2 min). It is interesting to note that when the lactone **2** was reacted with methanol–$FeCl_3$ in classical conditions (CH_2Cl_2, room temperature, 24 h), compound **5a** was obtained in a moderate yield (43%) together with methyl glucopyranosiduronate **4a** (26%). In MW conditions, **4a** would not be formed or alternatively the methyl acetal initially formed would be rapidly hydrolyzed. When we tested the action of $FeCl_3$ on compound **4a** under microwave conditions no cleavage at the anomeric center occurred. These results suggest that the chemoselectivity observed could be a consequence of microwave effects.

We have extended the selective ring opening of D-glucopyranosylurono-6,1-lactone **2** by introducing butyl, octyl, and dodecyl chains (Scheme 3). The results of reactions catalyzed by *p*-TsOH, $SnCl_4$, and $FeCl_3$ are summarized in Table 4.



Scheme 3.

In the case of *p*-TsOH, yields of alkyl glucofuranosidurono-6,3-lactone derivatives **1b–d** decreased with the chain length but stereoselectivity increased, for example, high β-selectivity was obtained for dodecyl compound **1d**.

With $SnCl_4$, in shorter reaction time (2 min), the 6,1-lactone **2** was totally converted into compounds **4b–d**. In previously reported work,[14] the $SnCl_4$-catalyzed coupling of silyl ethers with the 6,1-lactone **2** allowed to α-*O*-glucuronide derivatives in high stereoselectivity. No esterification of the carboxylic acid was observed in these classical conditions. Mechanistic pathways for the glycosydation reactions of the donor and the anomerization reactions of GlcA and related compounds in the presence of $SnCl_4$ are discussed, α-glucopyranosiduronates are formed by anomerization of β-anomers.[14,20c] Compared to classical heating, MW seems to accelerate this anomerization catalyzed by $SnCl_4$.Yields decreased slightly, the stereoselectivity increased with the chain length, with a high α-selectivity in dodecyl (dodecyl-D-glucopyranosid)uronate derivative **4d**.

Table 4. Reaction of compound **2** with alcohols/catalyst

ROH (6 equiv)	Catalyst	MW conditions[a]	Product (% yield, α/β)
Butanol	*p*-TsOH	105/95/10	**1b** (81, 20/80)
Octanol	*p*-TsOH	200/110/10	**1c**[9] (61, 15/85)
Dodecanol	*p*-TsOH	200/110/10	**1d**[9] (45, 5/95)
Butanol	$SnCl_4$	60/70/2	**4b** (91, 85/15)
Octanol	$SnCl_4$	30/60/2	**4c** (88, 90/10)
Dodecanol	$SnCl_4$	30/60/2	**4d** (85, 95/5)
Butanol	$FeCl_3$	60/65/3	**5b** (81)
Octanol	$FeCl_3$	60/70/3	**5c** (79)
Dodecanol	$FeCl_3$	60/60/3	**5d** (68)

[a] Power (Watts)/temperature (°C)/time (min).

3. Conclusion

When using $FeCl_3$ as catalyst, the chemoselectivity was in favor of esterified compounds **5b–d**; no glycosidation was observed in these conditions.

We have reported a rapid access to different D-glucuronic acid derivatives under microwave irradiation. The reactions present regioselectivities differing from those obtained using classical methods, especially when $SnCl_4$ and $FeCl_3$ are used as catalysts. With $FeCl_3$, the chemoselectivity in favor of esterified products **5a–d** allowed to obtain directly interesting synthetic intermediates. There are a number of multistep approaches described for the synthesis of **5a**, including the use of corresponding α-bromide[22] or anomeric acetate[23] more expensives than GlcA, but no general routes to other alkyl glucopyranuronates are reported. The MW solvent-free conditions described here give a rapid access to these important glucuronate synthons. Studies with other acceptors are currently under investigation.

4. Experimental

4.1. General

All chemicals were purchased from Aldrich or Acros (France). Thin-layer chromatography (TLC) was performed on silica gel 60 F_{254} (Merck) plates with visualization by UV light (254 nm) and/or charring with a vanillin–H_2SO_4 reagent. Preparative column chromatography was performed using 230–400 mesh Merck silica gel (purchased from Aldrich). Optical rotations were determined with a Jasco Dip 370 electronic micropolarimeter (10 cm cell). ^1H and ^{13}C NMR spectra were recorded on a Bruker 300 WB spectrometer at 300 and 75 MHz, respectively. Chemical shifts are given as δ values with reference to tetramethylsilane (TMS). Low resolution electrospray mass spectra (ESI-MS) in the positive ion mode were obtained on a Waters-Micromass ZQ quadrupole instrument, equipped with an electrospray (Z-spray) ion source (Waters-Micromass, Manchester, UK). High resolution electrospray experiments (ESI-HRMS) 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). All solvents were distilled before use. Microwave irradiation was performed in a CEM Discover® System.

4.2. 2,3,4-Tri-*O*-acetyl-D-glucopyranosylurono-6,1-lactone (2)

To a mixture of GlcA (3 g, 15.45 mmol) and I_2 (1.17 g, 4.46 mmol) in an open Pyrex flask was added acetic anhydride (11.7 mL, 123.77 mmol). The mixture was irradiated (300 W) at 115 °C for 10 min. The crude product was dissolved in CH_2Cl_2, then washed successively with saturated solution of $Na_2S_2O_3$, $NaHCO_3$, and NaCl. The organic layers were dried on Na_2SO_4, concentrated and a flash chromatography (cyclohexane/ethyl acetate 7:3) gave the lactone **2**[14] (4.29 g, 92%) as white solid. Mp 127 °C; NMR data were in accordance with the literature.[14]

4.3. General procedure for the synthesis of compounds 1b–5d

To a mixture of GlcA (200 mg, 1.03 mmol) or 6,1-lactone **2** (200 mg, 0.66 mmol) and alcohol (6 equiv) in an open Pyrex flask was added the catalyst (0.3 equiv for PTSA, 1 equiv for $FeCl_3$ or 1 equiv for $SnCl_4$). The flask was placed in the microwave reactor and irradiated (reaction time, irradiation power and assigned temperature are indicated in Tables 1, 3 and 4). Continuous stirring and heating of the semi-solid reaction mixture provided homogeneity of materials. The temperature was controlled all along the reaction and measured by an infrared detector. The crude was then chromatographed on silica gel by gradient elution with mixtures of cyclohexane and increasing amounts of ethyl acetate.

4.3.1. *n*-Butyl β-D-glucofuranosidurono-6,3-lactone (1b). Colorless syrup. Yield: 194 mg (81%, α/β:20/80); α and β isomers were isolated. β isomer: syrup, $[\alpha]_D^{20}$ −12.0 (*c* 0.14, CH_3OH); IR: 3273, 2351, 2342, 1797 cm^{-1}; ^1H NMR (CD_3OD) 5.02 (s, 1H, H-1), 4.84 (dd, 1H, *J*=6.5, 4.6 Hz, H-4), 4.82 (m, 3H, H-3, 2×OH), 4.51 (d, 1H, *J*=6.5 Hz, H-5), 4.22 (s, 1H, H-2), 3.83 (m, 1H, OCH_2), 3.33 (m, 1H, OCH_2), 1.50 (m, 2H, CH_2), 1.33 (m, 2H, CH_2), 0.92 (t, 3H, *J*=7.2 Hz, CH_3). ^{13}C NMR (CD_3OD) δ 175.8 (C6), 109.1 (C1), 83.4 (C3), 77.9 (C4), 77.2 (C2), 69.1 (C5), 69.6 (OCH_2), 31.0, 19.0 (2×CH_2), 12.9 (*C*H_3CH_2). α isomer: white solid, mp 73–74 °C; $[\alpha]_D^{20}$ +91.4 (*c* 1, CH_3OH); ^1H NMR (CD_3OD) 5.18 (d, 1H, *J*=4.5 Hz, H-1), 4.75 (m, 4H, H-3, H-4, 2OH), 4.57 (d, 1H, *J*=4.8 Hz, H-5), 4.23 (d, 1H, *J*=4.5 Hz, H-2), 3.81 (m, 1H, OCH_2), 3.56 (m, 1H, OCH_2), 1.61 (m, 2H, CH_2), 1.41 (m, 2H, CH_2), 0.92 (t, 3H, *J*=7.2 Hz, CH_3). ^{13}C NMR (CD_3OD) δ 176.9 (C6), 104.4 (C1), 86.6 (C3), 78.1 (C2), 76.9 (C4), 70.6 (C5), 69.8 (OCH_2), 32.6, 20.2 (2×CH_2), 14.2 (*C*H_3CH_2). HRMS [M+Na] calcd for $C_{20}H_{32}O_{10}Na$: 255.0855. Found [M+Na]: 255.0845.

4.3.2. Butyl (butyl 2,3,4-tri-*O*-acetyl-α,β-D-glucopyranosid)uronate (4b). Mixture of α, β isomers: colorless syrup. Yield: 260 mg (91%) α/β:85/15; $[\alpha]_D^{20}$ +81.1 (*c* 1, CH_2Cl_2). IR: 1756, 1224, 1044 cm^{-1}. α isomer: ^1H NMR ($CDCl_3$) δ 5.49 (t, 1H, *J*=9.5 Hz, H-3), 5.14 (d, 1H, *J*=9.5 Hz, H-4), 5.10 (d, *J*=3.7 Hz, H-1), 4.83 (dd, 1H, *J*=3.7, 9.5 Hz, H-2), 4.29 (d, 1H, *J*=10.0 Hz, H-5), 4.17–4.09 (m, 2H, CO_2CH_2), 3.72 (m, 1H, OCH_2), 3.43 (m, 1H, OCH_2), 2.03 (s, 3H, CH_3CO), 1.97 (s, 6H, 2×CH_3CO), 1.59 (m, 4H, 2×CH_2), 1.36 (m, 4H, 2×CH_2), 0.91 (t, 6H, *J*=7.3 Hz, 2×C*H*$_3CH_2$). ^{13}C NMR ($CDCl_3$) δ 169.9 (2×CO), 169.2 (CO), 167.7 (C6), 95.7 (C1), 70.5 (C2), 69.8 (C4), 69.6 (C3), 68.7 (OCH_2), 68.2 (C5), 65.7 (CO_2CH_2), 31.1 (CH_2), 30.2 (CH_2), 20.4 (3×*C*H_3CO), 18.9 (2×CH_2), 13.6 (2×*C*H_3CH_2). HRMS [M+Na] calcd for $C_{20}H_{32}O_{10}Na$: 455.1893. Found [M+Na]: 455.1889.

4.3.3. Octyl (octyl 2,3,4-tri-*O*-acetyl-α,β-D-glucopyranosid)uronate (4c). Mixture of α, β isomers: colorless syrup. Yield: 317 mg (88%); α/β:90/10; $[\alpha]_D^{20}$ +65.4 (*c* 1, CH_2Cl_2); IR: 2925, 2357, 1758, 1368, 1220, 1049 cm^{-1}. α isomer: ^1H NMR ($CDCl_3$) δ 5.50 (t, 1H, *J*=9.6 Hz, H-3), 5.15 (d, 1H, *J*=9.6 Hz, H-4), 5.10 (d, *J*=3.6 Hz, H-1), 4.85 (dd, 1H, *J*=3.6, 9.6 Hz, H-2), 4.30 (d, 1H, *J*=10.0 Hz, H-5), 4.15–4.02 (m, 2H, CO_2CH_2), 3.70 (m, 1H, OCH_2), 3.43 (m, 1H, OCH_2), 2.03 (s, 3H, CH_3CO), 1.99 (s, 6H, 2×CH_3CO), 1.58 (m, 4H, 2×CH_2), 1.25 (m, 20H, 10×CH_2), 0.86 (m, 6H, 2×C*H*$_3CH_2$). ^{13}C NMR ($CDCl_3$) δ 169.9 (2×CO), 169.3 (CO), 167.7 (C6), 95.7 (C1), 70.5 (C2), 69.7 (C4), 69.5 (C3), 69.0 (OCH_2), 68.2 (C5), 66.0 (CO_2CH_2), 31.7 (CH_2), 29.1 (CH_2), 28.2 (CH_2), 25.8 (CH_2), 25.6 (CH_2), 22.5 (CH_2), 20.5 (3×*C*H_3CO), 14.0 (2×*C*H_3CH_2). HRMS [M+Na] calcd for $C_{28}H_{48}O_{10}Na$: 567.3145. Found [M+Na]: 567.3148.

4.3.4. Dodecyl (dodecyl 2,3,4-tri-*O*-acetyl-α,β-D-glucopyranosid)uronate (4d). Mixture of α, β isomers: white solid. Yield: 369 mg (85%); α/β:95/5; $[\alpha]_D^{20}$ +68.2 (*c* 1, CH_2Cl_2); IR: 2925, 2856, 1755, 1222, 1044 cm^{-1}. α isomer: ^1H NMR ($CDCl_3$) δ 5.48 (t, 1H, *J*=9.8 Hz, H-3), 5.15 (t, 1H, *J*=9.5 Hz, H-4), 5.10 (d, 1H, *J*=3.4 Hz, H-1), 4.83 (dd, 1H, *J*=3.4, 10.0 Hz, H-2), 4.28 (d, 1H, *J*=10.0 Hz, H-5), 4.06–3.93 (m, 2H, CO_2CH_2), 3.61 (m, 1H, OCH_2), 3.33 (m, 1H, OCH_2), 1.97 (s, 3H, CH_3CO), 1.94 (s, 6H, 2×CH_3CO), 1.53 (m, 4H, 2×CH_2), 1.20 (m, 36H, 18×CH_2), 0.81 (m, 6H, 2×C*H*$_3CH_2$). ^{13}C NMR ($CDCl_3$) δ 169.8 (2×CO), 169.3 (CO), 167.7 (C6), 95.7 (C1), 71.1 (C2), 70.5 (C4), 69.6 (C3), 69.5 (OCH_2), 68.2 (C5), 66.0 (CO_2CH_2), 31.8 (CH_2), 29.3 (CH_2), 28.2 (CH_2), 25.8 (CH_2), 22.5 (CH_2), 20.4 (3×*C*H_3CO), 13.9 (2×*C*H_3CH_2). HRMS [M+Na] calcd for $C_{36}H_{64}O_{10}Na$: 679.4397. Found [M+Na]: 679.4396.

4.3.5. Butyl 2,3,4-tri-*O*-acetyl-D-glucopyranuronate (5b). Mixture of α, β isomers: colorless syrup. Yield: 202 mg (81%); α/β:85/15; $[\alpha]_D^{20}$ +71.3 (*c* 1, CH_2Cl_2); IR: 3469, 2963, 1751, 1370, 1219, 1038 cm^{-1}. α isomer: ^1H NMR ($CDCl_3$) δ 5.56 (t, 1H, *J*=9.8 Hz, H-3), 5.55 (d, 1H, *J*=3.5 Hz, H-1), 5.18 (t, 1H, *J*=9.8 Hz, H-4), 4.90 (dd, 1H, *J*=9.8, 3.5 Hz, H-2), 4.57 (d, 1H, *J*=10.0 Hz, H-5), 4.24 (d, 1H, *J*=3.5 Hz, OH), 4.17–4.09 (m, 2H, CO_2CH_2), 2.07 (s, 3H, CH_3CO), 2.02 (s, 6H, 2×CH_3CO), 1.59 (m, 2H, CH_2), 1.36 (m, 2H, CH_2), 0.91 (t, 3H, *J*=7.3 Hz, C*H*$_3CH_2$). ^{13}C NMR ($CDCl_3$) δ 170.1 (2×CO), 169.5 (CO), 168.2 (C6), 90.1 (C1), 71.1 (C2), 69.9 (C4), 69.7 (C3), 68.5 (C5), 66.5 (CO_2CH_2), 30.7 (CH_2), 21.1 (3×*C*H_3CO), 19.3 (CH_2), 14.0 (*C*H_3CH_2). HRMS [M+Na] calcd for $C_{20}H_{32}O_{10}Na$: 399.1257. Found [M+Na]: 399.1267.

4.3.6. Octyl 2,3,4-tri-*O*-acetyl-D-glucopyranuronate (5c). Mixture of α, β isomers: colorless syrup. Yield: 221 mg (79%); α/β:75/25; $[\alpha]_D^{20}$ +60.5 (*c* 1, CH_2Cl_2); IR: 3473, 2946, 1752, 1368, 1229, 1037 cm^{-1}. α isomer: ^1H NMR

($CDCl_3$) δ 5.55 (t, 1H, J=9.8 Hz, H-3), 5.54 (d, 1H, J=3.6 Hz, H-1), 5.16 (t, 1H, J=9.8 Hz, H-4), 4.89 (dd, 1H, J=9.8, 3.6 Hz, H-2), 4.56 (d, 1H, J=10.0 Hz, H-5), 4.15–4.02 (m, 2H, CO_2CH_2), 2.07 (s, 3H, CH_3CO), 2.01 (s, 6H, 2×CH_3CO), 1.60 (m, 2H, CH_2), 1.25 (m, 12H, 5×CH_2), 0.86 (m, 3H, CH_3CH_2). ^{13}C NMR ($CDCl_3$) δ 170.6 (2×CO), 169.9 (CO), 168.7 (C6), 90.6 (C1), 72.1 (C2), 69.9 (C4), 69.7 (C3), 68.5 (C5), 66.7 (CO_2CH_2), 32.1 (CH_2), 29.5 (CH_2), 28.7 (CH_2), 26.1 (CH_2), 23.0 (CH_2), 21.1 (3×CH_3CO), 14.4 (CH_3CH_2). HRMS [M+Na] calcd for $C_{28}H_{48}O_{10}Na$: 455.1893. Found [M+Na]: 455.1883.

4.3.7. Dodecyl 2,3,4-tri-*O*-acetyl-D-glucopyranuronate (5d). Mixture of α, β isomers: white solid. Yield: 220 mg (68%); α/β:85/15; $[\alpha]_D^{20}$ +54.1 (*c* 1, CH_2Cl_2); IR: 3448, 2917, 2848, 1732, 1346, 1228, 1055 cm^{-1}. α isomer: ^{1}H NMR ($CDCl_3$) δ 5.55 (t, 1H, J=9.8 Hz, H-3), 5.54 (d, 1H, J=3.5 Hz, H-1),, 5.19 (t, 1H, J=9.8 Hz, H-4), 4.91 (dd, 1H, J=9.8, 3.5 Hz, H-2), 4.57 (d, 1H, J=10.0 Hz, H-5), 4.16–3.97 (m,2H, CO_2CH_2), 3.85 (s, 1H, OH), 2.08 (s, 3H, CH_3CO), 2.02 (s, 6H, 2×CH_3CO), 1.53 (m, 2H, CH_2), 1.26 (m, 18H, 9×CH_2), 0.88 (m, 3H, CH_3CH_2). ^{13}C NMR ($CDCl_3$) δ 170.0 (2×CO), 169.4 (CO), 168.1 (C6), 90.2 (C1), 71.1 (C2), 69.9 (C4), 69.7 (C3), 68.5 (C5), 66.7 (CO_2CH_2), 32.3 (CH_2), 30.0 (CH_2), 29.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 28.8 (CH_2), 26.1 (CH_2), 23.1 (CH_2), 20.5 (3×CH_3CO), 14.0 (CH_3CH_2). HRMS [M+Na] calcd for $C_{36}H_{64}O_{10}Na$: 511.2519. Found [M+Na]: 511.2526.

Acknowledgements

The authors acknowledge the 'Conseil Régional de Picardie' (Programme Alternatives Végétales) for financial support.

References and notes

1. Loupy, A.; Petit, A.; Bogdal, D. *Microwaves in Organic Synthesis*; Wiley-VCH: Weinheim, Germany, 2002; pp 147–180.
2. Lidström, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225–9283.
3. Hamelin, J.; Bazureau, J. P.; Texier-Boullet, F. M. *Microwaves in Organic Synthesis*; Wiley-VCH: Weinheim, Germany, 2002; pp 253–293.
4. (a) Bougrin, K.; Loupy, A.; Soufiaoui, M. *J. Photochem. Photobiol., C: Photochem Rev.* **2005**, *6*, 139–167; (b) De la Hoz, A.; Diaz-Ortiz, A.; Langa, F. *Microwaves in Organic Synthesis*; Wiley-VCH: Weinheim, Germany, 2002; pp 295–343.
5. Corsaro, A.; Chiacchio, U.; Pistara, V.; Romeo, G. *Curr. Org. Chem.* **2004**, *8*, 511–538.
6. *Microwave Assisted Organic Synthesis*; Tierney, J. P., Lidström, P., Eds.; Blackwell Publishing: Oxford, UK, 2005.
7. Strauss, C. R.; Varma, R. S. *Top. Curr. Chem.* **2006**, *266*, 199–231.
8. (a) Leenders, G. G.; Damen, E. W. P.; Bitsterveld, E. J. A.; Sheeren, H. W.; Houba, P. H. J.; van der Meulen-Muilemen, I. H.; Boven, E.; Haisna, H. J. *Bioorg. Med. Chem.* **1999**, *7*, 1597–1610; (b) El Alaoui, A.; Saha, N.; Schmidt, F.; Monneret, C.; Florent, J. C. *Bioorg. Med. Chem.* **2006**, *14*, 5012–5019.
9. (a) Bertho, J. N.; Ferrières, V.; Plusquellec, D. *J. Chem. Soc., Chem. Commun.* **1995**, 1391–1393; (b) Ferrières, V.; Bertho, J. N.; Plusquellec, D. *Carbohydr. Res.* **1998**, *311*, 25–35.
10. Dax, K.; Weidmann, H. *Carbohydr. Res.* **1972**, *25*, 363–370.
11. (a) Limousin, C.; Cléophax, J.; Petit, A.; Loupy, A.; Lukacs, G. *J. Carbohydr. Chem.* **1997**, *16*, 327–342; (b) Loupy, A.; Régnier, S. *Tetrahedron Lett.* **1999**, *40*, 6221–6224; (c) Vo-Thanh, G.; Lahrache, H.; Loupy, A.; Kim, I. J.; Chang, D. H.; Jun, C. H. *Tetrahedron* **2004**, *60*, 5539–5543; (d) Naeimi, H.; Moradi, L. *Catal. Commun.* **2006**, *7*, 1067–1071.
12. (a) Perio, B.; Dozias, M. J.; Jacquault, P.; Hamelin, J. *Tetrahedron Lett.* **1997**, *38*, 7867–7870; (b) Paul, S.; Gupta, M.; Gupta, R.; Loupy, A. *Tetrahedron Lett.* **2001**, *42*, 3827–3829; (c) Selvi, S. T.; Nadaraj, V.; Mohan, S.; Sasi, R.; Hema, M. *Bioorg. Med. Chem.* **2006**, *14*, 3896–3903.
13. Takeda, Y.; Akimoto, T.; Kyogoku, Y. *Carbohydr. Res.* **1992**, *106*, 175–192.
14. Polakova, M.; Pitt, N.; Tosin, M.; Murphy, P. V. *Angew. Chem., Int. Ed.* **2004**, *43*, 2518–2521.
15. Das, S. K.; Reddy, K. A.; Rao, K. V. L. N.; Mukkanti, K. *Carbohydr. Res.* **2005**, *340*, 1387–1392.
16. Kartha, K. P. R.; Field, R. A. *Tetrahedron* **1997**, *53*, 11753–11766.
17. Arts, S. J. H. F.; van Rantwijk, F.; Sheldon, R. A. *J. Carbohydr. Chem.* **1996**, *15*, 317–319.
18. (a) Shanmugam, P.; Rajasingh, P. *Tetrahedron* **2004**, *60*, 9283–9295; (b) Shaabani, A.; Teimouri, M. B.; Samadi, S.; Soleimani, K. *Synth. Commun.* **2005**, *35*, 535–541; (c) Ferreira, V. F.; de Souza, M. C. B. V.; Rianelli, R. S.; da Silva, F. C.; Antunes, O. A. C. *Prog. Catal. Res.* **2005**, 147–175.
19. Trynda, A.; Madja, J.; Konitz, A.; Wisniewski, A. *Carbohydr. Res.* **2000**, *329*, 249–252.
20. (a) Velasco-Torrijos, T.; Murphy, P. V. *Org. Lett.* **2004**, *6*, 3961–3964; (b) Velasco-Torrijos, T.; Murphy, P. V. *Tetrahedron: Asymmetry* **2005**, *16*, 261–272; (c) O'Brien, C.; Polakova, M.; Pitt, N.; Tosin, M.; Murphy, P. V. *Chem.—Eur. J.* **2007**, *13*, 902–909.
21. Mieczkowski, J.; Zamojski, A. *Carbohydr. Res.* **1977**, *55*, 177–192.
22. (a) Fisher, B.; Nudelman, A.; Ruse, M.; Herzig, J.; Gottlieb, H. E. *J. Org. Chem.* **1984**, *49*, 4988–4993; (b) Iyer, S. S.; Rele, S. M.; Baskaran, S.; Chaikof, E. L. *Tetrahedron* **2003**, *59*, 631–638; (c) Rele, S. M.; Iyer, S. S.; Baskaran, S.; Chaikof, E. L. *J. Org. Chem.* **2004**, *69*, 9159–9170.
23. (a) Soliman, S. E.; Bassily, R. W.; El-Sokkary, R. I.; Nashed, M. A. *Carbohydr. Res.* **2003**, *338*, 2337–2340; (b) Pearson, A. G.; Kiefel, M. J.; Ferro, V.; von Itzstein, M. *Carbohydr. Res.* **2005**, *340*, 2077–2085; (c) Engstrom, K. M.; Daanen, J. F.; Wagaw, S.; Stewart, A. O. *J. Org. Chem.* **2006**, *71*, 8378–8383; (d) Chittaboina, S.; Hodges, B.; Wang, G. *Lett. Org. Chem.* **2006**, *3*, 35–39; (e) Engstrom, K. M.; Henry, R. F.; Marsden, I. *Tetrahedron Lett.* **2007**, *48*, 1359–1362.