Pergamon

Tetrahedron 56 (2000) 5877–5883

TETRAHEDRON

Synthesis of New Diols Derived from Dianhydrohexitols Ethers under Microwave-Assisted Phase Transfer Catalysis

Saber Chatti, Michel Bortolussi and André Loupy*

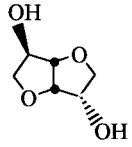
Laboratoire des Réactions Sélectives sur Supports, ICMO, UMR 8615, Bât. 410, Université Paris-Sud, 91405 Orsay Cedex, France

Received 26 April 2000; accepted 9 June 2000

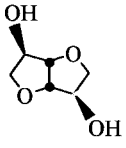
Abstract—Alkylation of mono-benzylated isosorbide and isomannide was performed under microwave assisted phase transfer catalysis (PTC). A small amount of solvent was necessary to provide good yields (90–96%) within 15 min. In order to minimize the competitive elimination, halide leaving group was changed to tosylate as competitive S_N2–E2 processes were involved. After removal of benzyl moiety by hydrogenation, a series of new diols from dianhydrohexitols were thus prepared.

Introduction

Biomass constitutes a renewable source of natural products used as unfailing starting materials for access to less polluting new compounds able to substitute petroleum derivatives. Among the important by-products of biomass are the dianhydrohexitols obtained from sugar industry by double dehydration of starch. These chiral compounds exist as two main isomers according to the relative configurations of their two hydroxyl functions[1,2] (isosorbide **A**, isomannide **B**, respectively, derived from D-glucose and D-mannose).



A



B

In spite of the interest of their structures and attractive properties, very few publications concern their use in macromolecular chemistry,[3–9] possibly due to their weak reactivity and selectivity problems resulting from the two different hydroxyl functions. They consist essentially in symmetrical polymers resulting from their reactions with dihalides, diamino dihydrochlorides, dicarboxylic acid dichlorides and diisocyanates.

Results and Discussion

We describe thus herein the synthesis of new diols from dianhydrohexitol moieties separated by ethers functions in order to be used further as starting monomers in polymerization reactions and able to lead to non-symmetrical compounds. The goal of these new molecules could be the access to some biodegradable chiral macromolecules with complexing properties.

They could be prepared from isosorbide **A** or isomannide **B** in a three-step procedure involving: (i) monobenzylation of one of the hydroxyl functions, (ii) alkylation with a difunctionalized alkylating agent, (iii) subsequent removal of benzyl moiety by hydrogenation (see Scheme 1).

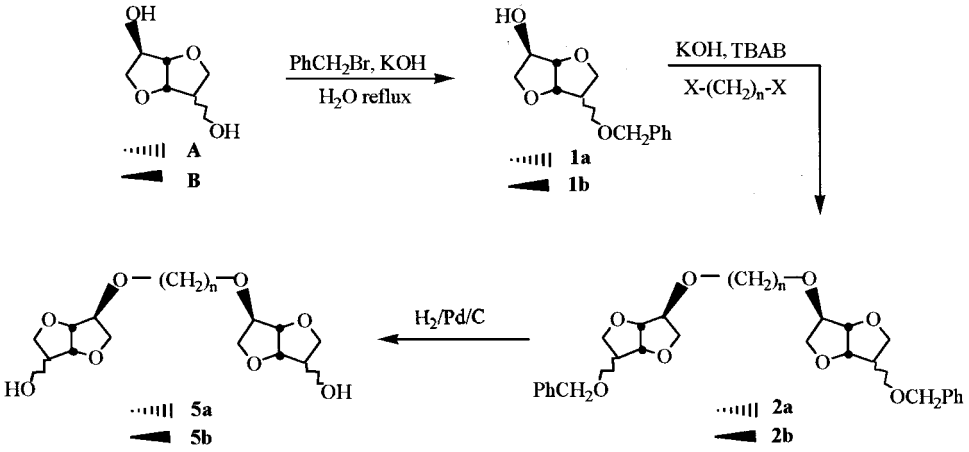
Selective mono-benzylations of **A** and **B** have been realized according to a previous work.[10] The so-obtained compounds were submitted to alkylation with α,ω-dihalides or ditosylates. As reported in a rather similar case, these reactions were performed under microwave (MW)-assisted phase transfer catalysis (PTC) using tetra-*n*-butylammonium bromide (TBAB) as a phase transfer agent.[11] To check the possibility of intervention of specific MW effects (non-purely thermal), the results obtained were compared with conventional heating using a thermostated oil bath at the same temperature and for similar reaction times. To this purpose, a monomode microwave reactor (Synthewave 402 from Prolabo) was used, allowing an accurate control of both temperature and emitted power, taking advantage of a homogeneous electromagnetic field (focused microwaves).

As a model reaction, conditions were optimized with mono-benzylated isosorbide and 1,8-dibromooctane (Table 1) according to our previous paper[11] dealing with the synthesis of diethers from dianhydrohexitols. Besides the expected ethers **1b**, some amounts of alkene **3a** were obtained resulting from a dehydrobromination on the common intermediate involved in S_N2–E2 competitive processes (see Scheme 2).

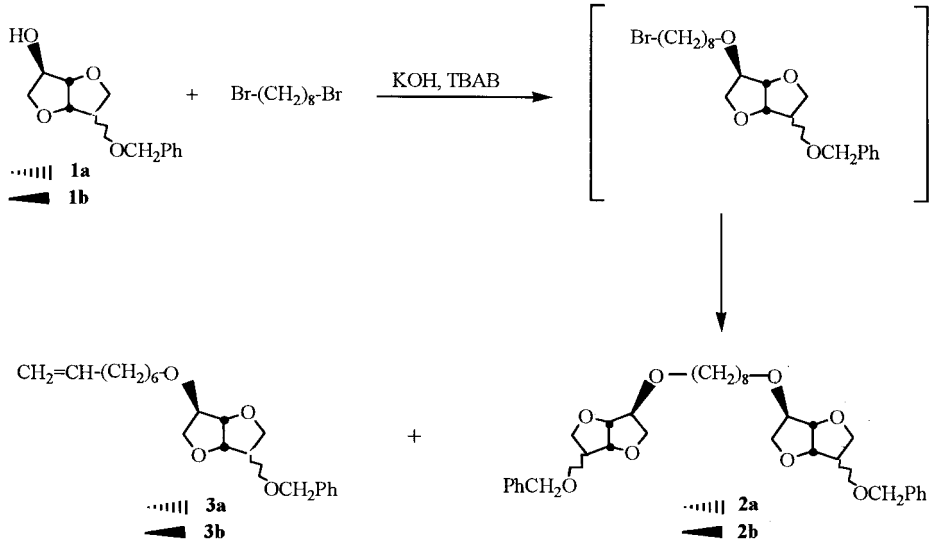
Keywords: dianhydrohexitols; microwaves; phase transfer catalysis (PTC); *O*-alkylation.

* Corresponding author. Tel.: +33-1-69-15-7650; fax: +33-1-69-15-4679; e-mail: aloupy@icmo.u-psud.fr

0040–4020/00/$ - see front matter
PII: S0040-4020(00)00539-1



Scheme 1.



Scheme 2.

The most convenient conditions (yields ~70%) involve the use of only 2% of catalyst in *p*-xylene for 5 min at 140°C or in toluene for 15 min at 110°C. Significant amounts (28–32%) of elimination by-products were obtained. These conditions were then extended to various aliphatic dibromides for both **1a** and **1b** with a change in molar ratio of reactants using a slight deficit of dibromide (Table 2).

With the aim to enlarge the scope of the study, we have examined the reaction with dialkyl chloride (in spite of their lower reactivity), generally cheaper and easily

Table 1. Reaction of **1a** (2 mmol) with 1,8-dibromooctane under MW in the presence of KOH and TBAB (relative amounts **1a**:base:X–R–X=2:3:1.5)

TBAB (%)	Solvent (0.25 mL)	Time (min)	Temperature (°C)	Yields[a] (%)		
				1a	**2a**	**3a**
1	*p*-Xylene	5	140	30	47	23
1	*p*-Xylene	30	140	10	70 (67)	20
2	*p*-Xylene	5	140	0	72 (68)	28
5	*p*-Xylene	5	140	2	70 (65)	28
2	Toluene	5	110	5	66 (62)	28
2	Toluene	15	110	0	68 (66)	32

[a] Yields were determined by ^{1}H NMR and given in brackets for isolated products.

Table 2. Reaction of **1a** or **1b** (2 mmol) with Br–$(CH_2)_n$–Br under MW in the presence of KOH and TBAB in toluene (0.25 mL) (relative amounts **1a**:base:dibromide:TBAB=2.5:2.5:1:0.02)

n	Time (min)	Yields[a] (%)					
		1a	**2a**	**3a**	**1b**	**2b**	**3b**
8	15	19	63	18	14	66	20
8	30	4	75	21	6	70	24
8	15[b]	33	55	12	30	52	18
8	30[b]	15	62	13	11	73	16
6	15	11	68	21	24	56	20
4	15	25	60	15	17	65	18

[a] Yields were determined by ^{1}H NMR.
[b] Reaction performed in refluxing cyclohexane (T=80°C).

Table 3. Reaction of **1a** or **1b** (2 mmol) with Cl–R–Cl under MW in the presence of KOH, NaBr and TBAB in toluene (0.25 mL) for 15 min (relative amounts **1a**:base:dichloride:TBAB=2.5:2.5:1:0.02)

R	NaBr	TBAB (%)	Yields[a] (%)					
			1a	**2a**	**3a**	**1b**	**2b**	**3b**
$(CH_2)_8$	−	20	55	29	16	49	32	19
$(CH_2)_8$	+	20	6	74	20	8	69	23
$(CH_2)_8$	+	2	37	47	16	39	42	19
$(CH_2)_8$	−	2[b]	71	27	2	69	28	3
$(CH_2)_8$	+	2[b]	64	35	1	64	33	3
$(CH_2)_8$	+	20[b]	30	56	14	28	55	17
$CH_2CH_2OCH_2CH_2$	+	20	12	70	18	13	71	16
$CH_2CH_2OCH_2CH_2$	+	2[b]	52	48	0	56	44	0
$(CH_2CH_2O)_2CH_2CH_2$	+	20	20	60	20	20	63	17

[a] Yields were determined by ^{1}H NMR.
[b] Reaction performed in refluxing cyclohexane (T=80°C).

commercially available when compared to their bromide equivalents. To enhance the possible complexing properties of the target-molecule, dichlorides from di- and tri-ethylene glycol were also used as alkylating agents (Table 3).

$$Cl–(CH_2CH_2O)_m–CH_2CH_2–Cl \qquad m = 1, 2$$

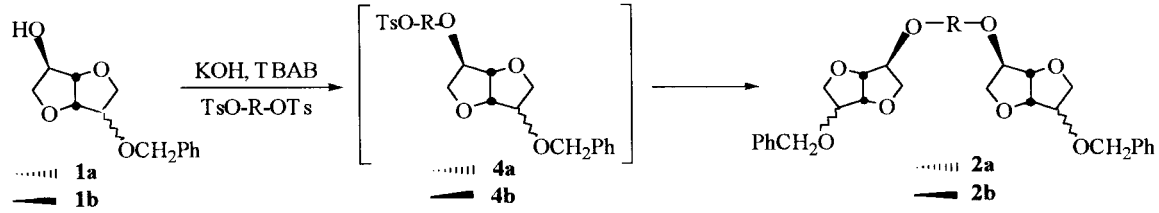
In order to improve the yields, reactions were performed in the presence of NaBr. It is here expected to favor halogen exchange from chloride to the more reactive bromide and to regenerate TBAB by ion-pair exchange[12] (Eqs. (1) and (2)).

$$R–Cl + n\text{-}Bu_4N^+, Br^- \rightarrow R–Br + n\text{-}Bu_4N^+, Cl^- \quad (1)$$

$$n\text{-}Bu_4N^+, Cl^- + Na^+, Br^- \rightleftharpoons n\text{-}Bu_4N^+, Br^- + Na^+, Cl^- \quad (2)$$

In refluxing toluene or cyclohexane for 15 min, good yields (60–74%) were obtained when the reaction was performed with 20% mol TBAB in the presence of an excess of NaBr.[11] When reactions were performed under classical heating (thermostated oil bath at 110 or 80°C) for 15 min, similar yields were obtained (compared to microwave), revealing thus the absence of any specific (non-purely thermal) effects of the radiation under these conditions.

Finally, in order to minimize the competitive elimination reaction leading to **3a** and **3b**, halide leaving group was changed to tosylate as more prone to avoid elimination and to favor nucleophilic substitution when a competition between S_N2 and E2 processes is involved[13] (Scheme 3; Table 4).



Scheme 3.

Table 4. Reaction of **1a** or **1b** (2 mmol) with TsO–R–OTs under MW in the presence of KOH and TBAB for 15 min (solvent=0.25 mL) (relative amounts **1**:base:ditosylate:TBAB=2.5:2.5:1:0.02)

R	T=110°C (toluene) Yields[a,b] MW (Δ)[c]		T=80°C (cyclohexane) Yields[a,b] MW (Δ)[c]	
	2a	**2b**	**2a**	**2b**
$(CH_2)_8$	95 (91)	84 (76)	96 (39)	95 (45)
$(CH_2)_6$	95 (90)	84 (84)	96 (40)	92 (42)
$(CH_2)_4$	91 (90)	92 (70)	96 (45)	91 (50)
$CH_2CH_2OCH_2CH_2$	92 (92)	90 (85)	91 (36)	89 (48)
$(CH_2CH_2O)_2CH_2CH_2$	90 (91)	91 (85)	90 (46)	92 (54)

[a] Yields for isolated products.
[b] Complement are monotosylates **4a** or **4b**.
[c] Results obtained by conventional heating (Δ) under the same conditions are given in brackets.

Yields were now considerably improved (up to 90–95%) due to disappearance of elimination products and leading also to a much more easy purification of **2a** and **2b**.

Due to high temperature level (110°C), the microwave specific effect was not appreciable in toluene and results remain identical with classical heating. When the temperature was lowered to 80°C changing toluene for cyclohexane (both non-polar solvents, i.e. transparent to microwave exposure), an important specific microwave effect appeared. In this case, good yields could be obtained only under microwave. The specific microwave effect was demonstrated when one considers the profiles of raising in temperature either under MW or Δ which were quasi-superposable whereas yields were clearly different (Fig. 1). Such a specific MW increasing effect as the temperature is decreased was described recently in the range 200–22°C

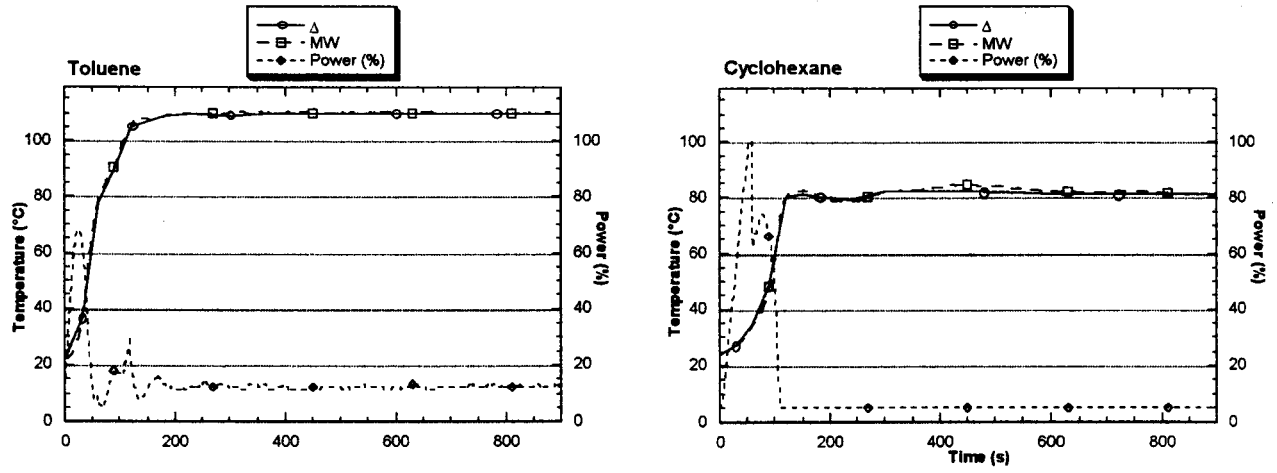


Figure 1. Profiles of raising in temperature and in emitted power for the reaction of monobenzylated isosorbide **1a** and ditosylate (n=8) (first line in Table 4).

(rate enhancements from 1.05–21.6) during the transformation of 2- and 4-tert-butylphenols catalyzed by clays in liquid phase.[14]

Continuous MW emission at power levels of 15–45 W (5–15% of the optimal value) was sufficient to keep constant the reactions at 80°C in cyclohexane and at 110°C in toluene.

Finally, catalytic hydrogenation of benzylated ethers **2a** and **2b** in ethanol or ethyl acetate with 10% palladium charcoal led, respectively, to ether diols **5a** and **5b** in excellent yields (90–96% for isolated products).

Conclusion

As a conclusion, various chiral alcohols linked by ether bridges derived from isosorbide and isomannide were synthesized under economic, easy-perform and mild conditions. The use of a small amount of non-polar solvent allowed the accurate control of temperature and could lead to specific (non-purely thermal) effects of microwave.

Experimental

Reactants and equipment

The different starting materials involved are purchased from Aldrich or Acros, and were used without any purification. Only isosorbide and isomannide [gift from Société Roquette-Frères (Lestrem, France)] were previously crystallized from acetone.

The microwave reactor was a monomode system (Synthewave 402 from Société Prolabo) with focused waves operating at 2.45 GHz. The temperature was controlled all along the reaction and evaluated by an infrared detector, which indicated the surface temperature (the IR lecture was calibrated by tuning the emissivity factor using a thermocouple introduced into the reaction mixture). Temperature was maintained constant at a choose value by modulation of emitted power. Mechanical stirring all along the irradiation provided a good homogeneity (power and temperature) and a data treatment, which was followed by a computer. All reactions were performed in cylindrical Pyrex open vessels. There is no need to use an upright condenser as only small amounts of solvent are involved and as the vessels walls remain at ambient temperature.

In order to compare microwave irradiation with conventional heating, the reactions were performed under similar experimental conditions (weight of reactants, time and temperature). When using a thermostated oil bath, the temperature was measured inserted with a Quick digital thermometer into the reaction mixture and the rate of the temperature rise was adjusted to be similar to that measured under microwave irradiation.

Flash column chromatography was performed using 35–70 μm silica gel (60) purchased from S.D.S. company. ^{1}H and ^{13}C NMR spectra were recorded at 200 and 51.32 MHz and at 250 and 62.91 MHz (Bruker WP 200, WP 250, respectively). Chemical shifts are given in ppm downfield from internal standard tetramethylsilane (δ=0.00 ppm). Melting points were measured on a Reichert apparatus and are uncorrected. Optical rotation were determined with a Perkin–Elmer 241 polarimeter.

General procedure for synthesis of the ditosylates

The diols (100 mmol) were dissolved in dry pyridine (200 mL) and cooled down to 0°C. A slight excess of *p*-toluenesulfonyl chloride (49.45 g, 230 mmol) was added over a period of 30 min and the reaction mixture stirred at 0°C for additional 3 h. It was poured into ice/H_2O (1 L) and 3 M HCl (50 mL) to give a white solid, which was recrystallized from absolute ethanol to give the ditosylates in 80–90% yields. All spectroscopic analysis (^{1}H and ^{13}C NMR) were in agreement with literature measurements.[15–18] 1,4-Bis-(toluene-4-sulfonyloxy)-butane (n=4): mp 70°C (lit.[18] mp 67.5–69.5°C); 1,6-bis-(toluene-4-sulfonyloxy)-hexane (n=6): mp 71°C (lit.[17] mp 71–72°C); 1,8-bis-(toluene-4-sulfonyloxy)-octane (n=8): mp 73°C (lit.[16] mp 72.8–73.3°C); bis-[2-(toluene-4-sulfonyloxy)-ethyl]ether

(m=1): mp 78°C (lit.[15] mp 78.5–79.3°C); 1,2-bis-[2-(toluene-4-sulfonyloxy)-4-ethoxy]ethane (m=2): mp 81°C (lit.[18] mp 81–82°C).

General procedure for the synthesis of 2a and 2b

Synthesis of **2a** and **2b** were performed under microwave irradiation or conventional heating. In a Pyrex cylindrical open reactor adapted to the Synthewave reactor, 2 mmol (0.5 g) of **1a** or **1b** were mixed with 1.6 mmol of alkyl halide (or tosylate), 0.004 mmol (0.014 g) of TBAB, 2 mmol of powdered KOH (0.140 g) [containing about 15% of water] and 0.25 mL of solvent. The mixture was then homogenized and submitted to microwave irradiation under mechanical stirring. It was cooled down to room temperature and diluted with 50 mL of methylene chloride. The solution was filtered (KOH in excess, mineral salts). The organic layer was concentrated under vacuum. Pure products (**2a** and **2b**) were isolated by liquid chromatography on silica gel with the adequate solvent system.

2a (n=8), isolated as a syrup; R_f 0.66 (pentane/EtOAc 1/1); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.3 (m, 4 CH_2, C-11 to C-12), 1.6 (m, 2 CH_2, C-10), 3.49 (m, 2H, H-6b), 3.61 (m, 4H, H-1b, H-6a), 3.96 (m, 10H, H-1a, H-2, H-5, H-9), 4.55 (m, 6H, H-3, H-7), 4.65 (dd, 2H, $J_{3,4}$=$J_{4,5}$=5 Hz, H-4), 7.30 (m, 10H, H-8); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 25.85 (CH_2, C-15), 29.27 (CH_2, C-14), 29.69 (CH_2, C-13), 69.96 (CH_2, C-12), 70.87 (C-1), 71.44 (C-6), 73.33 (C-7), 80.17 (C-4), 80.27 (C-5), 83.78 (C-2), 86.29 (C-3), 127.76 (C-11), 127.78 (C-10), 128.42 (C-9), 137.56 (C-8). Anal. Calcd for $C_{34}H_{46}O_8$: C, 70.10; H, 7.90; O, 22.00. Found: C, 69.53; H, 7.80; O, 22.63.

2a (n=6), isolated as a syrup; R_f 0.56 (pentane/EtOAc 1/1); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.3 (m, 2 CH_2, C-11), 1.6 (m, 2 CH_2, C-10), 3.49 (m, 2H, H-6b), 3.61 (m, 4H, H-1b, H-6a), 3.98 (m, 10H, H-1a, H-2, H-5, H-9), 4.56 (m, 6H, H-3, H-7), 4.65 (dd, 2H, $J_{3,4}$=$J_{4,5}$=5 Hz, H-4), 7.32 (m, 10H, H-8); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 25.65 (CH_2, C-14), 29.56 (CH_2, C-13), 69.60 (CH_2, C-12), 70.64 (C-1), 71.32 (C-6), 73.33 (C-7), 80.08 (C-4), 80.17 (C-5) 83.68 (C-2), 86.20 (C-3), 127.55 (C-11), 127.68 (C-10), 128.32 (C-9), 137.48 (C-8). Anal. Calcd for $C_{32}H_{42}O_8$: C, 69.31; H, 7.58; O, 23.10. Found: C, 69.21; H, 7.64; O, 23.14.

2a (n=4), isolated as a syrup; R_f 0.52 (pentane/EtOAc 1/1); ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.6 (m, 2 CH_2, C-10), 3.27 (m, 2H, H-6b), 3.45 (m, 4H, H-1b, H-6a), 3.99 (m, 10H, H-1a, H-2, H-5, H-9), 4.37 (m, 6H, H-3, H-7), 4.45 (dd, 2H, $J_{3,4}$=$J_{4,5}$=5 Hz, H-4), 7.13 (m, 10H, H-8); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 23.29 (CH_2, C-13), 69.77 (CH_2, C-12), 70.35 (C-1), 71.42 (C-6), 73.32 (C-7), 80.24 (C-4+C-5), 83.78 (C-2), 86.31 (C-3), 127.63 (C-11), 127.76 (C-10), 128.41 (C-9), 137.59 (C-8). Anal. Calcd for $C_{30}H_{38}O_8$: C, 68.44; H, 7.22; O, 24.33. Found: C, 68.36; H, 7.15; O, 24.49.

2a (m=1), isolated as a syrup; R_f 0.11 (pentane/EtOAc 1/1); ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.87 (m, 12H, 2 CH_2, H-1a, H-1b, H-6a, H-6b, H-10), 4.06 (m, 12H, 4 CH_2, H-2, H-5, H-9,), 4.56 (m, 6H, H-3, H-7), 4.77 (dd, 2H, $J_{3,4}$=$J_{4,5}$=5 Hz, H-4), 7.34 (m, 10H, H-8); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 69.77 (CH_2, C-12+C-13), 70.56 (C-1), 71.35 (C-6), 73.25 (C-7), 80.16 (C-4), 80.59 (C-5), 83.70 (C-2), 86.24 (C-3), 127.58 (C-11), 127.71 (C-10), 128.35 (C-9), 137.52 (C-8). Anal. Calcd for $C_{30}H_{38}O_9$: C, 66.42; H, 7.01; O, 26.56. Found: C, 66.31; H, 7.00; O, 26.69.

2a (m=2), isolated as a syrup; R_f 0.15 (pentane/EtOAc 1/1); ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.87 (m, 12H, 2 CH_2, H-1a, H-1b, H-6a, H-6b, H-11), 4.02 (m, 12H, 4 CH2, H-2, H-5, H-9, H-10), 4.55 (m, 6H, H-3, H-7), 4.78 (dd, 2H, $J_{3,4}$=$J_{4,5}$=5 Hz, H-3), 7.31 (m, 10H, H-8); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 69.84 (CH_2, C-14+C-13), 70.49 (CH_2, C-12), 70.51 (C-1), 71.39 (C-6), 73.29 (C-7), 80.23 (C-4), 80.76 (C-5), 83.76 (C-2), 86.26 (C-3), 127.62 (C-11), 127.75 (C-10), 128.40 (C-9), 137.58 (C-8). Anal. Calcd for $C_{32}H_{42}O_{10}$: C, 65.52; H, 7.16; O, 27.32. Found: C, 65.41; H, 7.12; O, 27.47.

2b (n=8), isolated as a syrup; R_f 0.69 (pentane/EtOAc 1/1); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.3 (m, 4 CH_2, C-11 to C-12), 1.6 (m, 2 CH_2, C-10), 3.45 (m, 2H, H-6b), 3.70 (m, 6H, H-1a, H-1b, H-6a), 4.00 (m, 8H, H-2, H-5, H-9), 4.50 (m, 6H, H-3, H-7), 4.75 (d, 2H, $J_{4,5}$=9.6 Hz, H-4), 7.30 (m, 10H, H-8). ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 25.83 (CH_2, C-15), 29.69 (CH_2, C-14), 30.90 (CH_2, C-13), 70.99 (CH_2, C-12), 71.06 (C-1, C-6), 72.38 (C-7), 79.31 (C-5, C-2), 80.37 (C-4), 80.48 (C-3), 127.85 (C-11, C-10), 128.85 (C-9), 137.69 (C-8). Anal. Calcd for $C_{34}H_{46}O_8$: C, 70.10; H, 7.90; O, 22.00. Found: C, 70.60; H, 8.10; O, 22.80.

2b (n=6), isolated as a syrup; R_f 0.61 (pentane/EtOAc 1/1); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.3 (m, 2 CH_2, C-11), 1.6 (m, 2 CH_2, C-10), 3.43 (m, 2H, H-6b), 3.71 (m, 6H, H-1a, H-1b, H-6a), 4.03 (m, 8H, H-2, H-5, H-9), 4.54 (m, 6H, H-3, H-7), 4.71 (d, 2H, $J_{4,5}$=9.6 Hz, H-4), 7.35 (m, 10H, H-8); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 25.62 (CH_2, C-14), 29.54 (CH_2, C-13), 70.66 (CH_2, C-12), 70.89 (C-1), 70.95 (C-6), 72.25 (C-7), 79.19 (C-5, C-2), 80.25 (C-4), 80.34 (C-3), 127.74 (C-11, C-10), 128.28 (C-9), 137.60 (C-8). Anal. Calcd for $C_{32}H_{42}O_8$: C, 69.31; H, 7.58; O, 23.10. Found: C, 69.20; H, 7.53; O, 23.25.

2b (n=4), isolated as a syrup; R_f 0.36 (pentane/EtOAc 1/1); ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.6 (m, 2 CH_2, C-10), 3.48 (m, 2H, H-6b), 3.70 (m, 4H, H-1a, H-1b, H-6a), 4.00 (m, 8H, H-2, H-5, H-9), 4.52 (m, 6H, H-3, H-7), 4.75 (d, 2H, $J_{4,5}$=9.6 Hz, H-4), 7.34 (m, 10H, H-8); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 26.14 (CH_2, C-13), 70.24 (CH_2, C-12), 70.89 (C-1, C-6), 72.20 (C-7), 79.14 (C-2+C-5), 80.23 (C-3, C-4), 127.68 (C-11, C-10), 128.23 (C-9), 137.57 (C-8). Anal. Calcd for $C_{30}H_{38}O_8$: C, 68.44; H, 7.22; O, 24.33. Found: C, 68.18; H, 7.20; O, 24.62.

2b (m=1), isolated as a syrup; R_f 0.10 (pentane/EtOAc 3/8); ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.75 (m, 12H, 2 CH_2, H-1a, H-1b, H-6a, H-6b, H-10), 4.01 (m, 12H, 4 CH2, H-2, H-5, H-9,), 4.52 (m, 6H, H-3, H-7), 4.70 (d, 2H, $J_{4,5}$=9.6 Hz, H-4), 7.34 (m, 10H, H-8); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 69.87 (CH_2, C-13), 70.65 (CH_2 C-12), 71.04 (C-1, C-6), 72.36 (C-7), 79.27 (C-2, C-5) 80.40 (C-4), 80.86 (C-3), 127.82 (C-11, C-10), 128.37 (C-9), 137.70 (C-8). Anal. Calcd for $C_{30}H_{38}O_9$: C, 66.42; H, 7.01; O, 26.56. Found: C, 65.51; H, 7.00; O, 27.49.

2b (m=2), isolated as a syrup; R_f 0.11 (pentane/EtOAc 3/8); ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.70 (m, 16H, 4 CH_2, H-1a, H-1b, H-6a, H-6b, H-10, H-11), 4.00 (m, 8H, 2 CH2, H-2, H-5, H-9,), 4.51 (m, 6H, H-3, H-7), 4.69 (d, 2H, $J_{4,5}$=9.6 Hz, H-4), 7.33 (m, 10H, H-8); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 69.80 (CH_2, C-14+C-13), 70.41 (CH_2, C-12), 71.10 (C-1, C-6), 72.32 (C-7), 79.35 (C-2, C-5) 80.49 (C-4), 80.81 (C-3), 127.76 (C-11, C-10), 128.40 (C-9), 137.85 (C-8). Anal. Calcd for $C_{32}H_{42}O_{10}$: C, 65.52; H, 7.16; O, 27.32. Found: C, 65.45; H, 7.10; O, 27.45.

General procedure for the deprotection of 2a and 2b

To a solution of starting material **2a** and **2b** in absolute ethanol or ethyl acetate (C=0.2 mol L^{-1}) was added palladium on charcoal (15%) and reaction was stirred under hydrogen atmosphere. After 3 h, the starting materials have disappeared. Filtration through celite, washing with adequate solvent and evaporation to dryness give a syrup.

5a (n=8) [solvent for hydrogenation: absolute ethanol]; R_f 0.52 (methanol/EtOAc 1/9); ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.3 (m, 4 CH_2, C-9 to C-10), 1.55 (m, 2 CH_2, C-8), 2.8 (m, 2H, OH), 3.50 (m, 6H, H-1b, H-6a, H-6b), 3.97 (m, 8H, 2 CH_2, H-1a, H-2, H-7), 4.25 (m, 2H, H-5), 4.45 (d, 2H, $J_{3,4}$=5 Hz, H-3), 4.65 (dd, 2H, $J_{3,4}$=$J_{4,5}$=5 Hz, H-4); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 25.77 (CH_2, C-10), 29.17 (CH_2, C-9), 29.62 (CH_2, C-8), 69.94 (CH_2, C-7), 70.90 (C-1), 75.77 (C-2), 76.49 (C-6), 80.01 (C-5), 80.23 (C-4), 88.26 (C-3). Anal. Calcd for $C_{20}H_{34}O_8$: C, 59.70; H, 8.45; O, 31.85. Found: C, 59.30; H, 8.40; O, 32.30.

5a (n=6) [ethyl acetate]; R_f 0.47 (methanol/EtOAc 1/9); $[\alpha]_D$=+103° (c 0.02, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.3 (m, 2 CH_2, C-9), 1.60 (m, 2 CH_2, C-8), 2.8 (m, 2H, OH), 3.51 (m, 6H, H-1b, H-6a, H-6b), 3.95 (m, 8H, 2 CH_2, H-1a, H-2, H-7), 4.25 (m, 2H, H-5), 4.45 (d, 2H, $J_{3,4}$=5 Hz, H-3), 4.65 (dd, 2H, $J_{3,4}$=$J_{4,5}$=5 Hz, H-4); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 25.61 (CH_2, C-9), 29.49 (CH_2, C-8), 69.87, (CH_2, C-7), 70.72 (C-1), 75.71 (C-2), 76.41 (C-6), 79.94 (C-5), 80.17 (C-4), 88.17 (C-3). Anal. Calcd for $C_{18}H_{30}O_8$: C, 57.75; H, 8.02; O, 34.22. Found: C, 57.47; H, 8.06; O, 34.43.

5a (n=4) [ethyl acetate]; R_f 0.40 (methanol/EtOAc 1/9); ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.60 (m, 2 CH_2, C-8), 2.8 (m, 2H, OH), 3.50 (m, 6H, H-1b, H-6a, H-6b), 4.00 (m, 8H, 2 CH_2, H-1a, H-2, H-7), 4.25 (m, 2H, H-5), 4.45 (d, 2H, $J_{3,4}$=5 Hz, H-3), 4.65 (dd, 2H, $J_{3,4}$=$J_{4,5}$=5 Hz, H-4); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 26.20 (CH_2, C-8), 69.91, (CH_2, C-7), 70.38 (C-1), 75.72 (C-2), 76.43 (C-6), 79.96 (C-5), 80.18 (C-4), 88.19 (C-3). Anal. Calcd for $C_{16}H_{26}O_8$: C, 55.49; H, 7.51; O, 37.00. Found: C, 55.40; H, 7.42; O, 37.18.

5a (m=1) [ethyl acetate]; R_f 0.21 (methanol/EtOAc 2/8); $[\alpha]_D$=+83 (c 0.07, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.8 (m, 2H, OH), 3.87 (m, 18H, 4 CH_2, H-1a, H-1b, H-2, H-6a, H-6b, H-7, H-8), 4.25 (m, 2H, H-5), 4.45 (d, 2H, $J_{3,4}$=5 Hz, H-3), 4.70 (dd, 2H, $J_{3,4}$=$J_{4,5}$=5 Hz, H-4); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 69.84 (CH_2, C-8+C-7), 70.62 (C-1), 75.74 (C-2), 76.28 (C-6), 80.02 (C-5), 80.66 (C-4), 88.12 (C-3). Anal. Calcd for $C_{16}H_{26}O_9$: C, 53.03; H, 7.18; O, 39.78. Found: C, 52.90; H, 7.12; O, 39.98.

5a (m=2) [ethyl acetate]; R_f 0.26 (methanol/EtOAc 2/8); ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.80 (m, 2H, OH), 3.85 (m, 22H, 6 CH_2, H-1a, H-1b, H-2, H-6a, H-6b, H-7, H-8, H-9), 4.25 (m, 2H, H-5), 4.45 (d, 2H, $J_{3,4}$=5 Hz, H-3), 4.70 (dd, 2H, $J_{3,4}$=$J_{4,5}$=5 Hz, H-4); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 69.90 (CH_2, C-9), 70.02 (CH_2, C-8), 70.49 (C-7), 70.69 (C-1), 75.78 (C-2), 76.38 (C-6), 80.06 (C-5), 80.71 (C-4), 88.19 (C-3). Anal. Calcd for $C_{18}H_{30}O_{10}$: C, 53.20; H, 7.40; O, 9.40. Found: C, 53.15; H, 7.35; O, 39.50.

5b (n=8) [absolute ethanol]; R_f 0.55 (methanol/EtOAc 1/9); ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.3 (m, 4 CH_2, C-9 to C-10), 1.60 (m, 2 CH_2, C-8), 2.95 (m, 2H, OH), 3.47 (m, 2H, H-6b), 3.70 (m, 6H, H-1a, H-1b, H-6a), 4.00 (m, 6H, H-2, H-7), 4.27 (m, 2H, H-5), 4.55 (m, 4H, H-4=H-3); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 25.78 (CH_2, C-10), 29.19 (CH_2, C-9), 29.64 (CH_2, C-8), 71.02 (CH_2, C-7), 71.34 (C-1), 72.15 (C-2), 74.94 (C-6), 80.00 (C-5), 80.58 (C-4), 81.77 (C-3). Anal. Calcd for $C_{20}H_{34}O_8$: C, 59.70; H, 8.45; O, 31.85. Found: C, 59.45; H, 8.40; O, 32.15.

5b (n=6) [absolute ethanol]; R_f 0.50 (methanol/EtOAc 1/9); $[\alpha]_D$=+105 (c 0.05, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.35 (m, 2 CH_2, C-9), 1.60 (m, 2 CH_2, C-8), 3.00 (m, 2H, OH), 3.47 (m, 2H, H-6b), 3.70 (m, 6H, H-1a, H-1b, H-6a), 4.00 (m, 6H, H-2, H-7), 4.27 (m, 2H, H-5), 4.55 (m, 4H, H-4=H-3); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 25.73 (CH_2, C-9), 29.62 (CH_2, C-8), 70.94 (CH_2, C-7), 71.37 (C-1), 72.16 (C-2), 75.04 (C-6), 80.03 (C-5), 80.62 (C-4), 81.80 (C-3). Anal. Calcd for $C_{18}H_{30}O_8$: C, 57.75; H, 8.02; O, 34.22. Found: C, 57.65; H, 8.00; O, 34.35.

5b (n=4) [absolute ethanol]; R_f 0.46 (methanol/EtOAc 1/9); ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.65 (m, 2 CH_2, C-8), 3.00 (m, 2H, OH), 3.47 (m, 2H, H-6b), 3.70 (m, 6H, H-1a, H-1b, H-6a), 4.00 (m, 6H, H-2, H-7), 4.27 (m, 2H, H-5), 4.55 (m, 4H, H-4=H-3); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 26.26 (CH_2, C-8), 70.49 (CH_2, C-7), 71.32 (C-1), 72.14 (C-2), 74.87 (C-6), 80.00 (C-5), 80.54 (C-4), 81.77 (C-3). Anal. Calcd for $C_{16}H_{26}O_8$: C, 55.49; H, 7.51; O, 37.00. Found: C, 54.17; H, 7.57; O, 38.25.

5b (m=1) [ethyl acetate]; R_f 0.25 (methanol/EtOAc 2/8); $[\alpha]_D$=+85 (c 0.01, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.00 (m, 2H, OH), 3.87 (m, 18H,4 CH_2, H-1a, H-1b, H-2, H-6a, H-6b, H-7, H-8), 4.25 (m, 2H, H-5), 4.55 (m, 4H, H-4=H-3); δ 69.89 (CH_2, C-8) 70.58 (CH_2, C-7), 71.39 (C-1), 72.13 (C-2), 74.77 (C-6), 80.38 (C-5), 80.63 (C-4), 81.74 (C-3). Anal. Calcd for $C_{16}H_{26}O_9$: C, 53.03; H, 7.18; O, 39.78. Found: C, 52.95; H, 7.15; O, 39.90.

5b (m=2) [ethyl acetate]; R_f 0.30 (methanol/EtOAc 2/8); ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.05 (m, 2H, OH), 3.85 (m, 22H, 6CH_2, H-1a, H-1b, H-2, H-6a, H-6b, H-7, H-8, H-9), 4.25 (m, 2H, H-5), 4.55 (m, 4H, H-4=H-3); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 69.93 (CH_2, C-9), 70.42 (CH_2, C-8), 70.51 (CH_2, C-7), 71.33 (C-1), 72.15 (C-2), 74.62 (C-6), 80.40 (C-5), 80.61 (C-4), 81.72 (C-3). Anal. Calcd

for $C_{18}H_{30}O_{10}$: C, 53.20; H, 7.40; O, 39.40. Found: C, 52.53; H, 7.27; O, 40.18.

Acknowledgements

We are grateful to Société Roquette-Frères (Lestrem, France) for a kind gift of dianhydrohexitols, and to the Higher Education Ministry of Tunisia for financial support.

References

1. Flèche, G.; Huchette, M. *Starch/Stärke* **1986**, *38*, 26.
2. Jacquet, F.; Gaset, A.; Gorrichon, J. P. *Inform. Chim.* **1984**, *246*, 155.
3. Majdoub, M.; Loupy, A.; Flèche, G. *Eur. Polym. J.* **1994**, *30*, 1431.
4. Bachmann, F.; Reimer, J.; Ruppenstein, M.; Thieme, J. *Macromol. Rapid. Commun.* **1998**, *19*, 21.
5. Cognet-Georjon, E.; Méchin, F.; Pascaut, J. P. *Makromol. Chem. Phys.* **1995**, *196*, 3733.
6. Kricheldorf, H. R.; Sun, S. T. *Makromol. Chem. Phys.* **1997**, *198*, 2197.
7. Storbeck, R.; Rehahn, M.; Ballauff, M. *Makromol. Chem.* **1994**, *194*, 53.
8. Stross, P.; Hemmer, R. *Adv. Carbohydr. Chem. Biochem.* **1991**, *49*, 93.
9. Thiem, J.; Bachmann, F. *Makromol. Chem.* **1991**, *192*, 2163.
10. (a) Loupy, A.; Monteux, D. *Tetrahedron Lett.* **1996**, *37*, 7023. (b) Abenhaim, D.; Loupy, A.; Munnier, L.; Tamion, R.; Marsais, F.; Quéguiner, G. *Carbohydr. Res.* **1994**, *261*, 255.
11. Chatti, S.; Bortolussi, M.; Loupy, A. *Tetrahedron Lett.* **2000**, *41*, 3367.
12. (a) Loupy, A.; Pardo, C. *Synthetic Commun.* **1988**, *18*, 1275. (b) Yufit, S. S.; Zinovyev, S. S. *Tetrahedron* **1999**, *55*, 6319. (c) Cohen, S.; Zoran, A.; Sasson, Y. *Tetrahedron Lett.* **1998**, *39*, 9815.
13. (a) Beltrame, P.; Biale, G.; Lloyd, D. J.; Parker, A. J.; Ruane, M.; Winstein, S. *J. Am. Chem. Soc.* **1972**, *94*, 2240. (b) Bartsch, R. A.; Bunnett, J. F. *J. Am. Chem. Soc.* **1969**, *91*, 1376. (c) Veeravagu, P.; Arnold, R. T.; Eigenmann, G. W. *J. Am. Chem. Soc.* **1964**, *86*, 3072.
14. Hajek, M.; Radoiu, M. Second World Congress on Microwave and Radio Frequency Processing, Orlando, USA, 2–6 April 2000. Comm. MWB-CP2-02.
15. Martin, A. E.; Bulkowski, J. E. *J. Org. Chem.* **1982**, *47*, 2314.
16. Streitwieser, A. *J. Am. Chem. Soc.* **1955**, *77*, 195.
17. Pear, E. J. P.; Thrower, J.; Veitch *J. Chem. Soc.* **1958**, 1322.
18. Curtis, W. D.; Laidler, D. A.; Stoddart, J. F.; Graham, H. J. *J. Chem. Soc., Perkin. Trans. 1* **1977**, 1756.