

Synthesis of diethers derived from dianhydrohexitols by phase transfer catalysis under microwave

Saber Chatti, Michel Bortolussi and André Loupy *

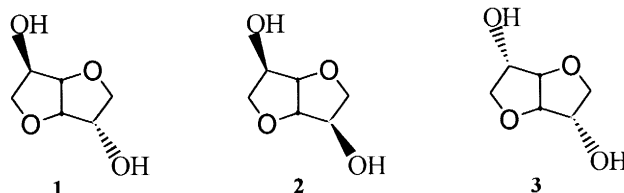
Laboratoire des Réactions Sélectives sur Supports, ICMO, UMR 8615, Bât. 410, Université Paris-Sud, 91405 Orsay Cedex, France

Received 20 December 1999; accepted 9 March 2000

Abstract

A series of new diethers were obtained by alkylation of dianhydrohexitols under microwave (MW) in phase transfer catalysis (PTC) conditions. The products were synthesized in good yields (>90%) within a few minutes. The yields are dramatically improved when compared to conventional heating under the same conditions, in spite of similar profiles of raising in temperature. © 2000 Published by Elsevier Science Ltd. All rights reserved.

1,4:3,6-Dianhydrohexitols are well-documented by-products of the starch industry, obtained by dehydration of D-hexitols.^{1,2} These chiral derivatives from biomass exist as three isomers according to the relative configuration of their two hydroxyl functions (isosorbide: **1**; isomannide: **2**; isoidide **3**, respectively derived from D-glucose, D-mannose and L-fructose). These compounds are serious candidates as starting materials. They could be interesting monomeric reagents for the synthesis of biodegradable polymers such as some polyesters,³ polyamides⁴ or polyurethanes.⁵ A main goal in our laboratory is to upgrade these biomass derivatives and to involve them in some polyalkylations.⁶ In order to optimize previous experimental conditions and to appreciate possible microwave effects on the polymerization,⁷ we have studied the di-*O*-alkylation with mono-alkylating agents under conditions of phase transfer catalysis (PTC), using concomitant microwave irradiation.⁸ Some di-*O*-alkylated products from isosorbide and isomannide have been described when using very reactive electrophilic reagents such as methyl iodide or sulfate, or allyl and benzyl bromide.^{2,9}

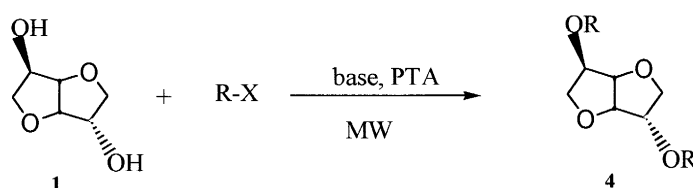


* Corresponding author. Fax: 33 1 69 15 46 79; e-mail: aloupy@icmo.u-psud.fr (A. Loupy)

We report here our main preliminary results dealing with optimization of alkylation of D-hexitols **1–3** under PTC conditions, either under microwave activation or by conventional heating, as it was yet described for the synthesis of the new furanic diethers from 2,5-furandimethanol.¹⁰

Microwave experiments were performed using a focused microwave reactor (monomode system: Synthewave 402[®] Prolabo).¹¹ Reactions were carried out in open vessels and temperatures were measured by an infrared detector which indicated the surface temperature (the IR emissivity was calibrated using an optical fiber introduced in the reaction mixture).

Dialkylation of isosorbide **1** involving *n*-octyl bromide (Scheme 1) was first examined under microwave irradiation (MW) with control of several significant parameters (Table 1) including different medium (using solvent-free conditions, a non-polar and a polar solvent), and bases and phase transfer agents (PTA).



Scheme 1.

Table 1
Reaction of **1** with $R-X=nC_8H_{17}Br$ under MW in the presence of a base and PTA [molar ratio=1:3:3:0.1]

Base	PTA	Solvent	t (min)	T (°C)	4 (%) ^{a)}
KOH	Aliquat 336	-	10	200	14
"	"	DMF	"	150	20
"	"	Xylene	"	140	40
"	"	"	60	"	90(80)
KOH	TBAB ^{b)}	"	5	"	96(86)
"	Crown-18,6	"	"	"	5
K ₂ CO ₃	TBAB ^{b)}	"	"	"	1
KOtBu	"	"	"	"	25

a) gc yield using an internal standard (dioctyl phthalate); yields in isolated products are indicated in brackets.

b) b) tetra-*n*-butylammonium bromide.

The best set of conditions (i.e. solid-liquid PTC in the presence of xylene using TBAB as phase transfer agent, 5 min)¹² were extrapolated to a series of various alkylating agents. In the optimal cases, in order to check the possible specific (non-purely thermal) MW effects, yields were compared with conventional heating (Δ) under the same conditions (Table 2).

From this table, it appears clearly that :

- excellent yields in diethers were obtained in all the cases examined under the optimal conditions determined with *n*-octyl bromide;
- alkyl chlorides need to be transformed in situ under PTC conditions in their bromide equivalents;¹³

Table 2
Reaction of **1** with several R-X using KOH and TBAB [relative amount 1:3:3:0.1] in xylene

R-X	t (min)	T (°C)	Yield 4 % ^{a)}	
			MW	Δ
$n\text{C}_8\text{H}_{17}\text{Br}$	5	140	96(90)	10
$n\text{C}_8\text{H}_{17}\text{Cl}$	"	"	32	2
$n\text{C}_8\text{H}_{17}\text{Cl} + \text{NaBr}^{\text{b)}}$	20	105	85(80)	40
$\text{C}_6\text{H}_5\text{CH}_2\text{Cl}$	5	125	98(90)	13
$3\text{Cl}-\text{C}_6\text{H}_4\text{CH}_2\text{Cl}$	"	"	95(90)	15
$4\text{Cl}-\text{C}_6\text{H}_4\text{CH}_2\text{Cl}$	"	"	96(89)	14
$3\text{F}-\text{C}_6\text{H}_4\text{CH}_2\text{Cl}$	"	"	95(90)	15
$\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_2\text{Br}^{\text{c)}}$	30	100	78(66)	45
$\text{CH}_3\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{Cl} + \text{NaBr}^{\text{c)}}$	40	"	76(68)	15

a) gc yields using an internal standard; yields in isolated products are given in brackets.

b) $1/\text{R-X}/\text{NaBr} = 1/4/4$

c) $1/\text{R-X} = 1/4$

- (iii) a very strong specific MW effect is involved in this reaction (comparison of MW and Δ yields). This effect is especially evident when one considers the rather similar profiles of raising in temperature (Fig. 1).

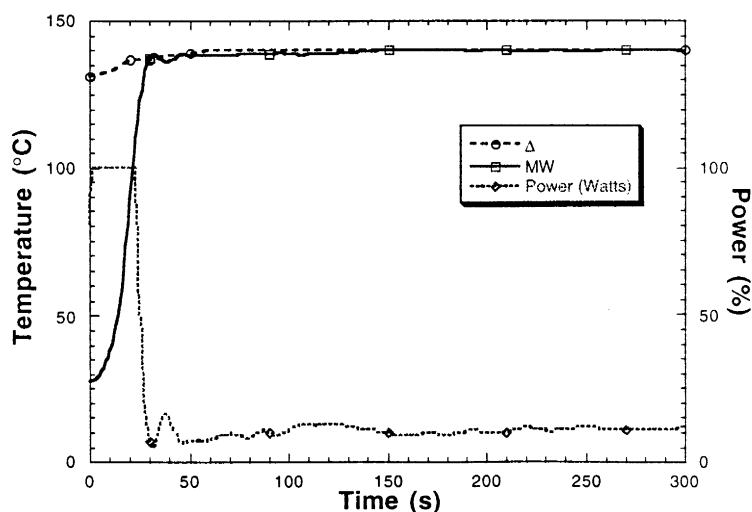


Fig. 1. Profiles of increase in temperature and power for reaction of **1** with $n\text{C}_8\text{H}_{17}\text{Br}$

Finally, the different D-hexitols **1–3** were tested under the optimal conditions indicated in Tables 1 and 2. The main results are given in Table 3.

We have described the synthesis of a series of chiral diethers derived from D-hexitols using a very efficient procedure. The presence of a rather small amount (1 mL for roughly 4 g of reactants) of an apolar solvent (xylene), is here of a great benefit as transparent to MW exposure and allowing a good control in temperature and medium viscosity.

Table 3
Dialkylation of D-hexitols with various alkylating agents using KOH and TBAB [relative amount 1:3:3:0.1] in xylene (GC yields)

R-X	t (min), T (°C)	1		2		3	
		MW (%)	Δ (%)	MW (%)	Δ (%)	MW(%)	Δ(%)
C ₆ H ₅ CH ₂ Cl	5, 125	98	13	98	15	97	20
nC ₈ H ₁₇ Br	5, 140	96	10	74	10	95	10
nC ₈ H ₁₇ Cl + NaBr	20, 105	85	40	83	35	85	60

Acknowledgements

We are grateful to Société Roquette-Frères (Lestrem, France) for a kind gift of D-hexitols.

References

- Flèche, G.; Huchette, M. *Starch/Stärke* **1986**, 38, 26.
- Stross, P.; Hemmer, R. *Adv. Carbohydr. Chem. Biochem.* **1991**, 49, 93.
- (a) Thiem, J.; Lüders, H. *Polym. Bull. (Berlin)* **1984**, 11, 365; *Starch/Stärke* **1984**, 36, 170. (b) Storbeck, R.; Rehahn, M.; Ballauff, M. *Makromol. Chem.* **1994**, 194, 53.
- Thiem, J.; Bachmann, F. *Makromol. Chem.* **1991**, 192, 2163.
- (a) Thiem, J.; Lüders, H. *Makromol. Chem.* **1986**, 187, 2775. (b) Cognet-Georjon, E.; Méchin, F.; Pascaut, J. P. *Makromol. Chem. Phys.* **1995**, 196, 3733. (c) Bachmann, F.; Reimer, J.; Ruppenstein, M.; Thiem, J. *Macromol. Rapid. Commun.* **1998**, 19, 21.
- Majdoub, M.; Loupy, A.; Flèche, G. *Eur. Polym. J.* **1994**, 30, 1431.
- (a) Jullien, H.; Petit, A.; Mérianne, C. *Polymer* **1996**, 37, 3319. (b) Singer, S. M.; Jow, J.; Delong, J. D.; Hawley, M. C. *Polym. Mater. Sci. Eng.* **1989**, 60, 869. (c) Hurduc, N.; Abdelyleah, D.; Busine, J. M.; Decock, P.; Surpateanu, G. *Eur. Polym. J.* **1997**, 33, 187.
- Deshayes, S.; Liagre, M.; Loupy, A.; Luche, J.-L.; Petit, A.; *Tetrahedron Lett.* **1999**, 55, 10851.
- (a) Abenhaim, D.; Loupy, A.; Munnier, L.; Tamion, R.; Marsais, F.; Quéguiner, G. *Carbohydr. Res.* **1994**, 261, 255. (b) Sageot, O.; Monteux, D.; Langlois, Y.; Riche, C.; Chiaroni, A. *Tetrahedron Lett.* **1996**, 37, 7019. (c) Loupy, A.; Monteux, D. *Tetrahedron Lett.* **1996**, 37, 7023.
- Majdoub, M.; Loupy, A.; Petit, A.; Roudesli, S. *Tetrahedron* **1996**, 52, 617.
- Loupy, A.; Petit, A.; Hamelin, J.; Texier-Boullet, F.; Jacquault, P.; Mathé, D. *Synthesis* **1998**, 1231.
- Typical procedure: In a pyrex cylindrical reactor adapted to the Synthwave reactor, 6.85 mmol (1 g) of D-hexitols were mixed with 20 mmol of alkyl halide, 1.4 mmol of TBAB, 20 mmol of powdered KOH (1.34 g) [containing about 15% of water] and 1 mL of solvent. The mixture was then homogenized and submitted to microwave under mechanical stirring for the adequate time. The temperature was measured by IR detection and controlled with an optical fiber throughout the reaction. It is maintained constant by modulation of the emitted power between 15 W and 300 W. The mixture was cooled down to room temperature and diluted with 40 mL of methylene chloride. The solution was filtered (KOH in excess, generated salts). The organic layer was then analyzed by GC after addition of an internal standard. In the best cases, pure products were isolated by liquid chromatography on silica gel (eluant: ethyl acetate/pentane mixtures).
- Loupy, A.; Pardo, C. *Synth. Commun.* **1988**, 18, 1275.