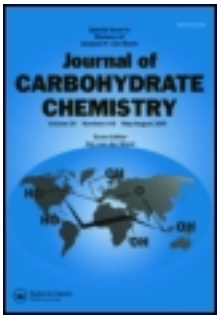


Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lcar20

Solvent-Free Synthesis of Decyl D-Glycopyranosides Under Focused Microwave Irradiation

C. Limousin [a] , J. Cléophax [a] , A. Petit [b] , A. Loupy [b] & G. Lukacs [a]
[a] Institut de Chimie des Substances Naturelles, C.N.R.S., Avenue de la Terrasse, 91198 Gif-sur-Yvette, France
[b] Laboratoire des Réactions Sélectives sur Supports, associé au C.N.R.S., ICMO, Université Paris-Sud bat. 410, 91405, Orsay, France
Published online: 19 Aug 2006.

To cite this article: C. Limousin , J. Cléophax , A. Petit , A. Loupy & G. Lukacs (1997): Solvent-Free Synthesis of Decyl D-Glycopyranosides Under Focused Microwave Irradiation, Journal of Carbohydrate Chemistry, 16:3, 327-342

To link to this article: http://dx.doi.org/10.1080/07328309708006533

J. CARBOHYDRATE CHEMISTRY, 16(3), 327-342 (1997)

SOLVENT-FREE SYNTHESIS OF DECYL D-GLYCOPYRANOSIDES UNDER FOCUSED MICROWAVE IRRADIATION

C. Limousin,[a] J. Cléophax,[a] A. Petit,[b] A. Loupy[b] and G. Lukacs[a]

[a]Institut de Chimie des Substances Naturelles, C.N.R.S.,
Avenue de la Terrasse, 91198 Gif-sur-Yvette, France

[b]Laboratoire des Réactions Sélectives sur Supports, associé au C.N.R.S., ICMO,
Université Paris-Sud bat. 410, 91405 Orsay, France

Received July 20, 1996 - Final Form February 6, 1997

ABSTRACT

A three step microwave assisted solvent-free synthesis of decyl D-glucopyranoside with 1-decanol was established for D-glucose and extended to D-galactose, D-mannose and *N*-troc-D-glucosamine with 70% average overall yield for the three steps (peracetylation, glycosylation and saponification). Rate enhancements and reduction of the reaction time were observed for the two last steps carried out under microwave irradiation when compared to conventional heating in the same conditions.

INTRODUCTION

Direct glycosylation of alcohols by monosaccharides remains an extensively investigated area.[1,2] Interest in alkyl or aryl glycosides is associated with their physical properties as liquid crystals, surfactants and their non-toxicity and easy

biodegradability.[3-5] The same properties are observed with polyglycoside analogues, such as alkyl polyglucosides (APG's) surfactants produced on a large scale by Henkel A. G.[6] The acid-catalyzed Fischer method for glycosylation of alcohols generally produces a mixture of glycosides. However it has been reinvestigated and considerable improvement has been realized.[7] For higher aliphatic alcohols, it is generally necessary to proceed by the intermediate preparation of butyl glycosides followed by transacetalization with a large excess of high alcohols at elevated temperature.[6,8] Multistep formation of glycosides is a widely used alternative which offers numerous possibilities concerning the nature of glycosyl donors, acceptors and activators.[9-13] Recently, this methodology has been applied to the synthesis of long-chain glycosides.[14]

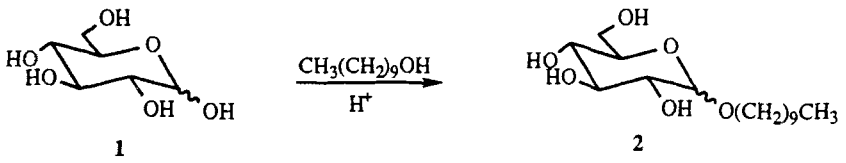
Microwave irradiation can be an efficient source of energy in synthetic organic chemistry,[15-19] and it has been applied also in carbohydrate chemistry.[20-24] Better results were obtained by coupling this technology with dry media techniques allowing efficient, economic, clean and safe synthetic conditions.[15,25] Dry media conditions and microwave irradiation allow working with open vessels and, with the very quick temperature increase, easy removal of volatile polar molecules and consequent displacement of the equilibrium. Two cases have been described in carbohydrate chemistry, the first deals with the conversion of glucans to 1,6-anhydroglucose but yields are low.[23] The second describes acetalization of L-galactono-1,4-lactone with long chain aldehyde over montmorillonites, where yields could be raised up to 89% (38% using a classical DMF-H_2SO_4/dry $CuSO_4$ system).[24]

Herein, we describe our attempts at glycosylation of 1-decanol with D-glucose by direct acid-catalysis and alternatively by a multistep procedure, under microwave irradiation with or without solid supports. The latter procedure was then extended to other sugars such as D-galactose, D-mannose and protected D-glucosamine. Our results were finally compared to conventional heating, all other conditions being equal, in order to evaluate non-thermal effects of microwaves.

RESULTS AND DISCUSSION

Direct glucosylation of 1-decanol with D-glucose.

In preliminary experiments, acid-catalyzed reaction of D-glucose with a slight (1.5 equiv) excess of 1-decanol was explored (Scheme 1). Acids tested were sulfuric acid or



Scheme 1

p-toluenesulfonic acid (TsOH), alone or in the presence of a variety of solid supports: Hyflo Super Cel[26] (HSC), celite, alumina, zeolites, montmorillonites, ion-exchange resins and florisil.

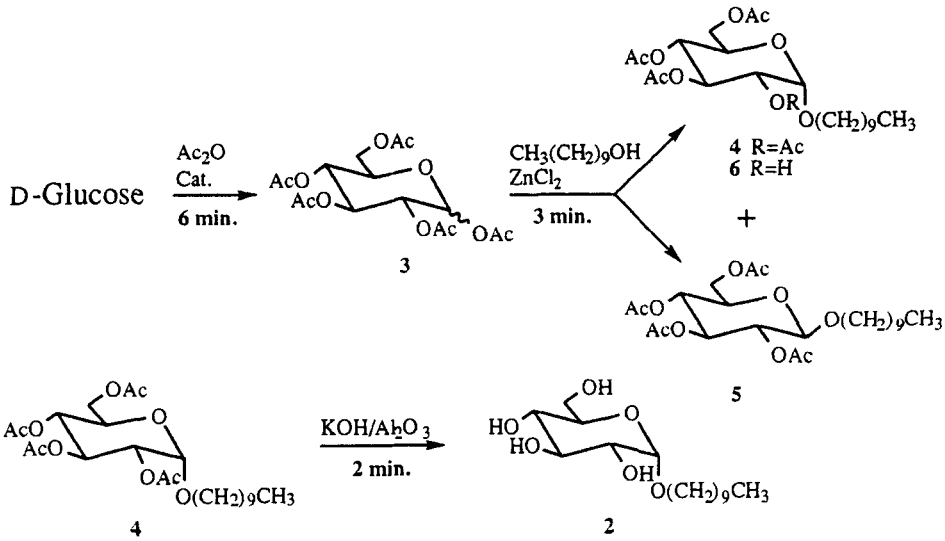
A maximum yield of 15% was observed after 10 min of microwave irradiation at a power of 200 to 20 watt and a final temperature of 150 °C with 0.5 equiv of TsOH, and adsorption of the reagents (2.5 g of D-glucose and 1.5 equiv of alcohol) on HSC. Among all solid supports tested, only HSC gave significant yields. It has little thermal influence on the behaviour of reactants because it absorbs microwaves only slightly.[27] The limitation in yields is mainly due to glucoside decomposition in the presence of acid under microwave irradiation.

These results were quite noteworthy in regard to reaction time and low excess of reagents when compared with results from the classical Fischer synthesis,[3] more recent adaptations using ion-exchange resins or cracking catalysts[7] and to enzyme-catalyzed glycosylations.[28] But the method was not totally satisfactory.

Three-step glycosylation of 1-decanol.

By analogy with an industrial process,[12] a three-step microwave assisted, high-yield glycosylation was carried out first with D-glucose: peracetylation of the sugar to penta-*O*-acetyl-D-glucopyranose, Lewis acid-catalyzed reaction with 1-decanol and then deacetylation (Scheme 2).

Peracetylation. Peracetylation of D-glucose (1 to 6 g) under microwave irradiation with a small excess (9 equiv) of acetic anhydride catalyzed by anhydrous potassium or sodium acetate (1.1 equiv) or zinc chloride (0.13 equiv) was practically quantitative in less than 15 min (Table 1, entries 1, 3, 5). As under classical conditions with AcONa or AcOK, reactions were highly β-selective (entries 4-6). With $ZnCl_2$, a 1/1 mixture of α/β pentaacetates was obtained under microwave irradiation whereas the ratio was 7/3 under conventional oil bath heating (entries 1, 2).



Scheme 2

Table 1 : Peracetylation of D-glucose (**1**), D-galactose (**11**), D-mannose (**15**) (6 g) and *N*-troc-D-glucosamine (**7**) (1.3 g) with acetic anhydride (9 equiv) and various catalysts. M. W.: microwave irradiation, C. H.: conventional heating.

Entry	Compd	Catalyst	Heating mode	Power (W)	Time (min)	Final T (°C)	Yield (%)	Ratio α / β
1	**1**	$ZnCl_2$ (0.13 equiv)	M. W.	50-20 W	6.5	125	98	1 / 1
2	**1**	$ZnCl_2$ (0.13 equiv)	C. H.		6.5	125	83	7 / 3
3	**1**	AcONa (1.1 equiv)	M. W.	80-20 W	10	106	90	2 / 8
4	**1**	AcONa (1.1 equiv)	C. H.		10	106	88	2 / 8
5	**1**	AcOK (1.1 equiv)	M. W.	80-20 W	15	135	80	3 / 7
6	**1**	AcOK (1.1 equiv)	C. H.		15	135	98	2 / 8
7	**7**	AcONa (1.1 equiv)	M. W.	80-20 W	11	140	97	6 / 4
8	**11**	AcONa (1.1 equiv)	M. W.	80-20 W	11	137	90	4 / 6
9	**15**	AcONa (1.1 equiv)	M. W.	80-20 W	11	127	87	8 / 2

When the same proportions of reagents were heated with an oil bath for the same time and at the final temperature reached by microwave irradiation, the yields were similar by the two means of heating. The most important point is that, *in both cases,* nearly quantitative yields were obtained within very short times with low reagent excesses. Attempts with *N*-troc-D-glucosamine **7** (1.3 g), D-galactose **11** (6 g) or D-mannose **15** (6 g) and sodium acetate as catalyst gave also excellent yields within 11 min (Table 1, entries 7, 8 and 9).

Glucosylation of 1-decanol. Glucosylation of 1-decanol (1.5 equiv) with penta-*O*-acetyl-D-glucopyranose (**3**) was attempted in the presence of several Lewis acids. Among a large variety of tested catalysts were $ZnSO_4$, $Zn(OTf)_2$, MgF_2, $FeCl_3$, $CoCl_2$, $CuCl_2$, $CeCl_3$, $MgCl_2$, $LiPF_6$, TsOH. Only $ZnCl_2$, $ZnBr_2$ and $SnCl_2$ afforded the expected glucosides in noteworthy yields (Table 2).

With $ZnCl_2$, various reaction parameters such as irradiation time and power, another salt or solid support addition and the molar ratio of $ZnCl_2$/sugar were studied. When 0.5 equiv or 2 equiv of $ZnCl_2$ were used, only 4 or 7% yields were obtained, respectively. An optimum quantity of 1 equiv of $ZnCl_2$ gave the best result: a 74% maximum yield of a mixture of α and β pyranosides was isolated with the α isomer as the major product (Table 2, entries 8 and 10).

It was noted that the reaction was effective only above 100 °C but not allowing the temperature to exceed 130 °C. Some partial deacetylation occurred during the irradiation. When the irradiation time was extended to 15 min, the amount of decyl 3,4,6-tetra-*O*-acetyl D-glucopyranoside glucoside **6** rose to 42% instead of 21% after 3 min. This result could constitute a good method for access to **6**. Therefore, in order to evaluate the glycosylation yields in Table 2, the crude mixture was reacetylated prior to separation.

With the same reagent proportions as in entry 10 (Table 2) but with oil bath heating (entry 11), no reaction was noticed within 10 min. Only a 25% yield of glucosides (21% α, 4% β) was isolated after 5 hours at 113 °C and reacetylation of the crude mixture as some deacetylation products, in particular compound **6**, were also observed. With an oil bath, 6 minutes were necessary to reach 113 °C whereas this temperature was obtained within 3 minutes under microwave irradiation (Figure). During conventional heating, the temperature was measured all along the reaction with a thermocouple inside the reaction mixture and during microwave heating, with an infrared detector. This difference in temperature increase is not sufficient to explain such variations in yields even after 5 hours with oil bath heating unless considering specific non-thermal effects of microwave

Table 2: $ZnCl_2$ catalyzed glucosylation of 1-decanol (1.5 equiv) with penta-*O*-acetyl-D-glucopyranose (**3**) (1.95 g), with or without solid supports addition.

Entry	Catalyst [a]	Power (W)	Time (min)	Final T (°C)	Total yield(%)	Ratio **4 / 5**
1	TsOH : 0.1 equiv	60-20 W	5	136	7	5 / 2
2	$SnCl_2$: 1 equiv	60-20 W	4	156	31	24 / 7
3	$ZnCl_2$ / Silica gel (1 g / 5 g)	100-20 W	11	100	30	16 / 14
4	$ZnCl_2$ / K 10 (1 g / 1.4 g)	100-20 W	3.5	135	33	24 / 9
5	Clayzic (b)	150-20 W	11	115	20	16 / 4
6	$ZnCl_2$ / sand (1 g / 5 g)	60-20 W	8.5	125	58	30 / 28
7	$ZnCl_2$ + sand (1 g / 7 g)	60-20 W	8	118	68	53 / 15
8	$ZnCl_2$ + HSC (c)	150-20 W	9	116	**74**	**64 / 9**
9	$ZnCl_2$ + HSC (d)	150-20 W	15	115	35	15 / 20
10	$ZnCl_2$: 1 equiv	60-20 W	3	113	**74**	**64 / 9**
11	$ZnCl_2$: 1 equiv	OIL BATH	10 300	113 113	0 25 [e]	 21 / 4

(a) $ZnCl_2$ / support = $ZnCl_2$ adsorbed on solid support - $ZnCl_2$ + support = $ZnCl_2$ dispersed with solid support with 1 equiv $ZnCl_2$ / sugar in both cases.
(b) Clayzic is $ZnCl_2$ adsorbed on montmorillonite K10.
(c) 1-decanol adsorbed on Hyflo Super Cel in ratio 1/8 ; $ZnCl_2$ = 1 equiv.
(d) 1-decanol and sugar adsorbed on Hyflo Super Cel in ratios 1/8 and 1/5 respectively; $ZnCl_2$ = 1 equiv.
(e) With 9% of *N*-(tetra-*O*-acetyl-α-D-glucopyranosyl)-pyridinium chloride.

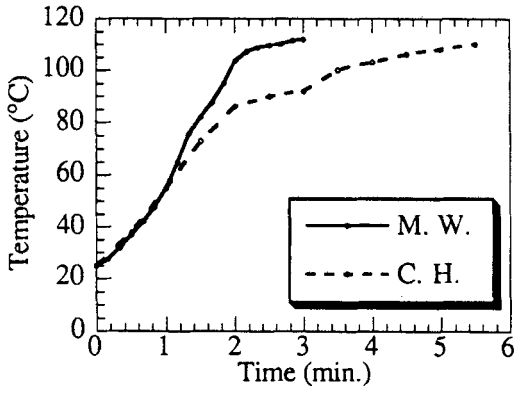


Figure: Glucosylation of 1-decanol with **3**. Comparison between microwave irradiation (M. W.) and conventional heating (C. H.).

Table 3: Saponification of decyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (**4**) (1.09 g) in dry media with various reagents.
M. W.: microwave irradiation, C. H.: conventional heating.

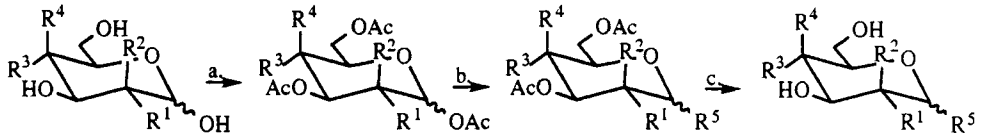
Entry	Reagents	Heating mode	Power (W)	Time (min)	Final T (°C)	Yield (%)
1	Al_2O_3	M. W.	200-20 W	15	133	< 2
2	KF / Al_2O_3 (a)	M. W.	200-20 W	3	152	< 2
3	KOH + Al_2O_3 (b)	M. W.	40-20 W	6	122	60
4	KOH / Al_2O_3 (c)	M. W.	40-20 W	3	116	79
5	KOH / Al_2O_3 (d)	M. W.	40-20 W	2	97	**86**
6	KOH / Al_2O_3 (d)	C. H.		2	100	<2

(a) KF adsorbed on alumina (1 g/ 5 g) KF/ sugar 5 / 1.
(b) KOH dispersed with alumina, KOH / sugar 5 / 1.
(c) KOH adsorbed on alumina (1 g / 3 g), KOH / sugar 4 / 1.
(d) KOH adsorbed on alumina (1 g / 3 g), KOH / sugar 5 / 1.

irradiation. Moreover, we showed that *N*-(tetra-*O*-acetyl-α-D-glucopyranosyl)-pyridinium chloride[29] was formed in 9% yield *only* with oil bath heating after reacetylation of the crude mixture. The formation of this additional product could be explained only if different mechanisms occurred under microwave irradiation and classical heating conditions. The tetra-*O*-acetyl-α-D-glucopyranosyl chloride should be formed as intermediate with oil bath heating and then reacted with pyridine (used for reacetylation), as mentioned.[29]

Saponification. No reaction was observed by microwave irradiation of adsorbed penta-acetate **4** on alumina (Varma's conditions[30]), but saponification of the protected glucoside **4** to decyl D-glucoside **2** was realized, in dry media, in the presence of a small excess of KOH adsorbed on alumina. In only 2 min under microwave irradiation, the deacetylation was practically quantitative (Table 3, entry 5).

The effect of microwave irradiation was here highly decisive since with conventional heating no reaction occurred after 2 min at 100 °C with the same reagent quantities (entry 6). By extending the reaction time up to 3 hours, only mixtures of partially deacetylated products were obtained.



7 R^1=NHTroc, R^2=R^3=H, R^4=OH
8 R^1=NHTroc, R^2=R^3=H, R^4=OAc
9 R^1=NHTroc, R^2=R^3=H, R^4=OAc, R^5=$O(CH_2)_9CH_3$
10 R^1=NHTroc, R^2=R^3=H, R^4=OH, R^5=$O(CH_2)_9CH_3$

11 R^1=R^4=OH, R^2=R^3=H
12 R^1=R^4=OAc, R^2=R^3=H
13 R^1=R^4=OAc, R^2=R^3=H, R^5=$O(CH_2)_9CH_3$
14 R^1=R^4=OH, R^2=R^3=H, R^5=$O(CH_2)_9CH_3$

15 R^1=R^4=H, R^2=R^3=OH
16 R^1=R^4=H, R^2=R^3=OAc
17 R^1=R^4=H, R^2=R^3=OAc, R^5=$O(CH_2)_9CH_3$
18 R^1=R^4=H, R^2=R^3=OH, R^5=$O(CH_2)_9CH_3$

a. Ac_2O, Cat. - b. $CH_3(CH_2)_9OH$, $ZnCl_2$ - c. KOH/Al_2O_3

Scheme 3

The glycosylation and saponification steps could be carried out successively without purification of the intermediate glycosides. A mixture of α and β-glucosides was isolated in an overall yield of 71% for these two steps.

Extension to other hexoses.

The same acetylation, glycosylation and saponification procedures were applied to 2-deoxy-2-(2,2,2-trichloroethoxy-carbonylamino)-D-glucose (**7**), D-galactose (**11**) and D-mannose (**15**) (Scheme 3).

Peracetylation of all three compounds was nearly quantitative in 11 min under microwave irradiation with AcONa as catalyst (Table 1, entries 7,8,9).

Reaction of the peracetates **8**, **12**, **16** with 1-decanol (1.5 equiv) and $ZnCl_2$ (1 equiv) gave 74, 73 and 77% of glycosides **9**, **13**, **17** respectively (Table 4). Irradiation times had to be adjusted for each peracetylated hexose. The ratio between α and β anomers was maximum for the mannoside **17**, as expected, and less favorable for the glucosamine derivative **9**. In related described glycosylations under conventional heating using zinc salts or other Lewis acids,[31,32] the selectivity was better, especially for the D-glucosamine derivatives, but the mechanism was probably different since activators such as trimethylsilyl bromide or trityl halides combined with zinc salts [$ZnBr_2$, $ZnCl_2$, $Zn(OTf)_2$] seemed to be necessary. The 1-halo intermediate was probably involved in these cases and not with microwave promoted reactions.

Table 4: Glycosylation of 1-decanol (1.5 equiv) with **8** (2.53 g), **12** (1.95 g), and **16** (1.95 g), and $ZnCl_2$ (1 equiv).

Entry	Compound	Microwave conditions P(W)-time(min)	Final T (°C)	Total yield (%)	α / β (%)
1	**8**	80-20 W, 15	112	**74**	**44 / 30**
2	**12**	60-20 W, 6	101	**73**	**54 / 17**
3	**16**	100-20 W, 6.5	100	**77**	**73 / 4**

CONCLUSION

By association of microwave irradiation and solvent-free reactions, a three step efficient glycosylation procedure of a long chain alcohol with hexoses was carried out. Reaction times were very short (maximum 15 min for the two first steps and 2 min for the third one). All reagents were easily accessible and used in very small excesses. Yields were good. For example, with D-glucose as starting compound, the overall yield for the three steps was 70%.

Moreover, specific, non purely thermal microwave effects seemed to be involved in the two last steps. Yields were very significantly increased under strictly the same experimental conditions by microwave irradiation when compared to conventional heating (from 0 to 74% for the glycosylation and from 0 to 96% for saponification). Otherwise, when the reaction time was extended with oil bath heating for the glycosylation step, by-products were formed in noticeable yields.

The origin of microwave effects could result from i) the more rapid rate of temperature increase, ii) best homogeneity in temperature, iii) modifications in activation parameters; $\Delta H^{\neq}$ and $\Delta S^{\neq}$ decreases have been shown.[19]

It is noteworthy that specific microwave effects described in the literature mainly concern solvent-free procedures.[33] Some publications claimed, on the contrary, the absence of specific activation: they essentially deal with reactions in organic solvents.[34] Interestingly, in other cases, important specific microwave effects were shown in apolar solvents.[35]

EXPERIMENTAL

General methods and equipment. Microwave irradiations were performed by means of a monomode reactor (Synthewave 402 from Prolabo) with focused waves. All reactions were performed in a cylindrical Pyrex vessel. The mixtures were introduced into the monomode reactor at the powers and times indicated in tables and stirred all along the irradiation to allow a better homogeneity. Temperatures were recorded throughout the reactions using an infrared detector connected to the reactor[36] which evaluates the surface temperature. The emissivity is then calibrated in accordance with a thermocouple or an optical Luxtron fiber inside the reaction mixture. A good agreement between the two measurements can then be recorded during the evolution of the reaction.

Flash column chromatography was performed using 35-70 μ silica gel (60) purchased from S.D.S. company. TLC was run using DC-Plastikfolien, silica gel F_{254} (Schleicher and Schuell), detection by UV light (254 nm) and by heating after sulfuric acid treatment. ^1H and ^{13}C spectra were recorded at 200 MHz and 50.33 MHz, at 250 MHz and 62.91 MHz and at 300 MHz and 75.49 MHz (Bruker WP 200, WP 250, WP 300 respectively). Tetramethylsilane was the internal standard (δ = 0.00 ppm). Melting points were measured on a Reichert apparatus and are uncorrected. Optical rotations were determined with a Perkin-Elmer 241 polarimeter. For described compounds, ^1H NMR values were in accordance with published ones. In addition, ^{13}C NMR values were given for some derivatives and $[\alpha]_D$ values were compared with literature data.

Direct glucosylation of 1-decanol with D-glucose (1). D-glucose (**1**) (143 mg, 0.77 mmol) and TsOH (77 mg, 0.4 mmol) were dissolved in water (5 mL) and Hyflo Super Cel (HSC) (1.35 g) was added; water was removed under vacuum. 1-Decanol (265 mg, 1.68 mmol) was dissolved in CH_2Cl_2, HSC (2 g) was added and CH_2Cl_2 was removed under vacuum. The two mixtures were mixed and stirred under microwave irradiation over 10 min (P: 200-20 W, final temperature: 150 °C). After cooling, the mixture was diluted with CH_3OH, filtered through a silica gel cake, washed with CH_3OH and the filtrate was concentrated under vacuum. Flash-chromatography (eluent: EtOAc/EtOH 9/1) afforded **2** as α and traces of β-anomer[13] mixture (38 mg, 15%). A white solid was obtained by precipitation from pentane. Difficulty was encountered in crystallizing since it has a tendency to separate out as gel.

Decyl α-D-glucopyranoside (**2**): ^{13}C NMR (62.9 MHz, CD_3OD) δ ppm: 99.9 (C-1), 74.9 (C-5), 73.4 (C-2, C-3), 71.5 (C-4), 69.2 (C-1'), 62.4 (C-6), 32.9, 30.6, 30.4, 27.2, 27.0, 23.6 (CH_2 alkyl chain), 14.5 (C-10' CH_3 alkyl chain).

Peracetylation of D-glucose (1).

a) Peracetylation of **1** catalyzed by AcONa (Table 1, entries 3, 4): **1** (1.5 g, 8.06 mmol), acetic anhydride (7.4 g, 72.5 mmol) and anhydrous AcONa (727 mg, 8.87 mmol) were stirred;

i) under microwave irradiation (P: 80-20 W, final *T* : 106 °C) over 10 minutes.

ii) with thermostated oil bath heating over 10 min at 106 °C.

In both cases, the mixture was poured into ice cold water, the peracetates precipitated as a mixture of α and β anomers. By microwave assisted acetylation, after filtration and crystallization from EtOH, 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (**3**) was isolated (2.26 g, 72%) and the α-anomer (565 mg, 18%) remained in the mother liquor. With oil bath heating, yields were 74% of β-anomer and 14% of α-anomer.

b) Peracetylation of **1** catalyzed by AcOK (Table 1, entries 5, 6): **1** (2 g, 11 mmol), acetic anhydride (10.2 g, 0.1 mol) and anhydrous AcOK (1.2 g, 12.1 mmol) were reacted by the two procedures - microwave irradiation: 80-20 W, final *T* : 135 °C or - oil bath heating: 135 °C over 15 minutes. Overall yield of peracetates (see a): 80% (3.43 g, 52% of β-anomer and 28% of α-anomer) by microwave heating and 98% (4.20 g, 82% of β-anomer and 16% of α-anomer) by oil bath heating.

c) Peracetylation of **1** catalyzed by $ZnCl_2$ (Table 1, entries 1, 2): **1** (2 g, 11 mmol), acetic anhydride (10.2 g, 0.1 mol) and anhydrous $ZnCl_2$ (200 mg, 1.47 mmol) were stirred under microwave irradiation (P: 50-20 W, final *T*: 125 °C) or with oil bath heating (*T*: 125 °C) over 6.5 minutes in both cases. The mixture was then diluted with EtOAc and filtered through a silica gel cake, the filtrate was concentrated under vacuum and the residue crystallized from EtOH. 98% Yield (4.23 g of 1/1 α/β-anomers) was obtained with microwave irradiation instead of 83% (3.58 g, α/β ratio 2.37/1.21) by conventional heating.

Glucosylation with penta-*O*-acetyl-D-glucopyranose (3), and $ZnCl_2$, followed by reacetylation.

1) Under microwave irradiation (Table 2, entry 10). Penta-*O*-acetyl-D-glucopyranose (**3**) (1.95 g, 5 mmol) and anhydrous $ZnCl_2$ (680 mg, 5 mmol) were mixed and 1-decanol (1.19 g, 7.5 mmol) was added. After 3 min under microwave irradiation (P: 60-20 W, final *T*: 113 °C), the reaction mixture was diluted with EtOAc, filtered through a silica gel cake and the filtrate was concentrated under vacuum. The residue was reacetylated with acetic anhydride (2.5 mL) in anhydrous pyridine (5 mL) over 3 h at room temperature. Water was added to the mixture followed by extraction with CH_2Cl_2 (2 x 30 mL) and the organic phases were washed with a saturated aqueous sodium

hydrogencarbonate solution. The organic layer was dried over magnesium sulfate, filtered and concentrated to give a crude mixture of α and β-anomers which were purified by flash chromatography (heptane/EtOAc 8/2 then heptane/EtOAc 7/3) to afford decyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (**4**) (1.56 g, 64%) and decyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**5**) (244 mg, 10%), respectively.

Data for **4**: $[\alpha]_D$ +110 (*c* 1.44, $CHCl_3$). Lit.[14a] $[\alpha]_D$ +111.9 (*c* 2, CH_2Cl_2). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm: 170.5-169.5 (4 O<u>C</u>OCH$_3$), 95.6 (C-1), 70.9 (C-2), 70.3 (C-3), 68.7 (C-1', C-4), 67.1 (C-5), 61.9 (C-6), 31.8, 29.5, 29.2, 22.6 (CH_2 alkyl chain), 20.6 (OCO<u>C</u>H$_3$), 14.0 (C-10', CH_3 alkyl chain).

Data for **5**: $[\alpha]_D$ -15 (*c* 1.19, $CHCl_3$). Lit.[13] mp 47.5-48.5, $[\alpha]_D$ -21.5 (CH_3OH). Lit.[14a] $[\alpha]_D$ = -7.6 (*c* 2, CH_2Cl_2). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm: 170.5-169.5 (4 O<u>C</u>OCH$_3$), 100.9 (C-1), 73.0 (C-3), 71.9 (C-5), 71.5 (C-2), 70.3 (C-1'), 68.6 (C-4), 62.1 (C-6), 32.0, 29.7, 29.5, 25.9, 22.7 (CH_2 alkyl chain), 20.7 (OCO<u>C</u>H$_3$), 14.2 (C-10', CH_3 alkyl chain).

2) With oil bath heating (Table 2, entry 11). **3** (1.95 g, 5 mmol) and anhydrous $ZnCl_2$ (680 mg, 5 mmol) were mixed, 1-decanol (1.19 g, 7.5 mmol) was added and this mixture was heated to 110 °C in a thermostated oil bath. After 10 min under stirring, no glucoside was detectable by TLC. After 5 h at 110 °C and then reacetylation of the crude mixture as in 1), glucosides **4** and **5** (611 mg, 25%, **4/5**: 21/4) and *N*-(tetra-*O*-acetyl-α-D-glucopyranosyl)pyridinium chloride (198 mg, 9%) were isolated.

Glucosylation with 3 under microwave irradiation for 14 min: 3 (1.95 g, 5 mmol) and anhydrous $ZnCl_2$ (680 mg, 5 mmol) were mixed in a flask, 1-decanol (1.19 g, 7.5 mmol) was added and this mixture was submitted to microwave irradiation for 15 min (P: 60-20 W, final *T* : 118 °C). The reaction mixture was diluted with EtOAc, filtered through a silica gel cake and the filtrate was concentrated under vaccum and submitted to flash chromatography: α and β glucosides **4**, **5** (690 mg, 28%) and decyl 3,4,6-tri-*O*-acetyl-α-D-glucopyranoside (**6**) (946 mg, 42%) were isolated.

Data for **6**: $[\alpha]_D$ +91 (*c* 0.87, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$) δ ppm: 5.25 (t, 1H, $J_{2,3} \sim J_{3,4}$ = 9.5 Hz, H-3), 5.0 (t, 1H, $J_{4,5}$ = 9.5 Hz, H-4), 4.9 (d, 1H, $J_{1,2}$ = 4 Hz, H-1), 4.27 (dd, 1H, $J_{5,6}$ = 5 Hz, $J_{6,6'}$ = 12 Hz, H-6), 4.05 (dd, 1H, $J_{5,6'}$ = 2.4 Hz, H-6'), 3.95 (m, 1H, H-5), 3.73 (m, 1H, H-1'a), 3.65 (m, 1H, H-2), 3.5 (m, 1H, H-1'b), 2.05 (q, 12H, 4 OCOC<u>H</u>$_3$), 1.6, 1.3, 0.9 (m, 2H, 14H, 3H, alkyl chain). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm: 171.1-170.7 (4 O<u>C</u>OCH$_3$), 98.3 (C-1), 73.7 (C-3), 70.9 (C-2), 69.0 (C-1'), 68.2 (C-4), 67.7 (C-5), 62.1 (C-6), 31.9, 29.6, 29.4, 26.2, 22.7 (CH_2 alkyl chain), 20.7 (4 OCO<u>C</u>H$_3$), 14.1 (C-10', CH_3 alkyl chain).

Anal. Calcd for $C_{22}H_{38}O_9$: C, 59.17; H, 8.58. Found: C, 59.45; H, 8.68.

Saponification of decyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (4) (Table 3, entry 5): KOH (10 g) was dissolved in water and adsorbed on alumina (30 g). Water was removed by evaporation under vacuum. Compound **4** (1.09 g, 2.24 mmol) was added to the KOH/Al_2O_3 powder (2.91 g i.e., 11.2 mmol KOH) and the reaction mixture was stirred over 2 min under microwave irradiation (P: 40 W, final *T* : 97 °C). The reaction mixture was diluted with CH_3OH, filtered through a silica gel cake and washed with CH_3OH. The filtrate was concentrated and separated by flash-chromatography (eluent: EtOAc/EtOH 9/1) to give α-anomer **2** (699 mg, 96%) as a precipitate from pentane.

Peracetylation of *N*-troc-D-glucosamine (7), D-galactose (11) and D-mannose (15). *N*-troc-D-glucosamine (**7**) (1.3 g, 3.3 mmol), D-galactose (**11**) or D-mannose (**15**) (6 g, 32.2 mmol) were acetylated with acetic anhydride (9 equiv) and anhydrous AcONa (1.1 equiv) under microwave irradiation for 11 min (Table 1, entries 7, 8, 9). 1,2,3,4,6-Penta-*O*-acetyl-β-D-galactopyranose (**12**) was crystallized from EtOH as the major product (6.78 g) and α-anomer remained in the mother liquor (4.52 g) for an overall yield of 90%. **16** (10.92 g, 87% from **15**) was obtained with high α-selectivity (ratio α/β 8/2 determined by NMR) and **8** (1.67 g, 97% from **7**) with a lower selectivity (ratio α/β 6/4 determined by NMR).

Glycosylation of 1-decanol with 8, 12, 16 and $ZnCl_2$. As described previously for derivative **3**, compounds **9**, **13**, **17** were obtained after 15, 6 or 6.5 min respectively under microwave irradiation at powers indicated in Table 4.

Decyl 2-deoxy-3,4,6-tri-*O*-acetyl-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (**9α**) and its β-anomer (**9β**) were obtained in ratio 44/30 (2.30 g, 74% overall yield).

Data for **9α**: $[\alpha]_D$ +73 (*c* 2, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$) δ ppm: 5.25 (t, 1H, $J_{2,3} = J_{3,4} = 9.5$ Hz, H-3), 5.1 (t, 1H, $J_{4,5} = 9.5$ Hz, H-4), 4.85 (d, 1H, $J_{1,2} = 3.6$ Hz, H-1), 4.7 (q, 2H, NH-CO-OC$\underline{H}_2$CCl$_3$), 4.25 (dd, 1H, $J_{5,6} = 4.5$ Hz, $J_{6,6'} = 12$ Hz, H-6), 4.1 (m, 2H, H-6', H-2), 4.0 (m, 1H, H-5), 3.7 (m, 1H, H-1'a), 3.45 (m, 1H, H-1'b), 2.05 (q, 9H, 3 OCOC$\underline{H}_3$), 1.6, 1.3, 0.9 (m, 2H, 14H, 3H, alkyl chain). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm: 170.8-169.6 (3 O$\underline{C}$OCH$_3$), 154.1 (NH-$\underline{C}$O-OCH$_2$CCl$_3$), 97.3 (C-1), 74.7 (NH-CO-O$\underline{C}$H$_2$CCl$_3$), 71.3 (C-3), 68.9 (C-1'), 68.4 (C-4), 67.8 (C-5), 62.1 (C-6), 54.1 (C-2), 32.0, 29.7, 29.4, 26.2, 22.8 (CH_2 alkyl chain), 20.8 (OCO$\underline{C}$H$_3$), 14.2 (CH_3 alkyl chain).

Anal. Calcd for $C_{25}H_{40}O_{10}Cl_3N$: C, 48.35; H, 6.49; Cl, 17.13; N, 2.26. Found: C, 48.34; H, 6.54; Cl, 17.17; N, 2.45.

Data for **9β**: $[\alpha]_D$ +9 (*c* 0.6, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$) δ ppm: 5.3 (t, 1H, $J_{2,3} \sim J_{3,4}$ = 9.5 Hz, H-3), 5.1 (t, 1H, $J_{4,5}$ = 9.5 Hz, H-4), 4.7 (m, 3H, H-1, NHCO-OC$\underline{H}_2$CCl$_3$), 4.3 (dd, 1H, $J_{5,6}$ = 5 Hz, $J_{6,6'}$ = 12 Hz, H-6), 4.1 (dd, 1H, $J_{5,6'}$ = 2 Hz, H-6'), 3.9 (m, 1H, H-1'a), 3.7 (m, 1H, H-5), 3.6 (m, 1H, H-2), 3.5 (m, 1H, H-1'b), 2.05 (q, 9H, 3 OCOC$\underline{H}_3$), 1.6, 1.3, 0.9 (m, 2H, 14H, 3H, alkyl chain). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm: 170.8-169.6 (3 O$\underline{C}$OCH$_3$), 154.1 (NH-$\underline{C}$O-OCH$_2$CCl$_3$), 100.9 (C-1), 74.6 (NH-CO-O$\underline{C}$H$_2$CCl$_3$), 72.0 (C-3), 71.8 (C-5), 70.5 (C-1'), 68.9 (C-4), 62.3 (C-6), 56.4 (C-2), 32.0, 29.7, 29.5, 25.9, 22.8 (CH_2 alkyl chain), 20.7 (OCO$\underline{C}$H$_3$), 14.2 (CH_3 alkyl chain).

Anal. Calcd for $C_{25}H_{40}O_{10}Cl_3N$: C, 48.35; H, 6.49; Cl, 17.13; N, 2.26. Found: C, 48.61; H, 6.51; Cl, 16.93; N, 1.99.

Decyl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside (**13α**) and its β-anomer (**13β**) were obtained in ratio 54/19 (1.78 g, 73% overall yield).

Data for **13α**: $[\alpha]_D$ +118 (*c* 1.1, $CHCl_3$). Lit.[14b]. ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm: 170.4-170.1 (4 O$\underline{C}$OCH$_3$), 96.1 (C-1), 68.7 (C-1'), 68.3 (C-2), 68.2 (C-4), 67.8 (C-3), 66.2 (C-5), 61.9 (C-6), 31.9, 29.6, 29.4, 26.1, 22.7 (CH_2 alkyl chain), 20.7 (4 OCO$\underline{C}$H$_3$), 14.1 (CH_3 alkyl chain).

Data for **13β**: $[\alpha]_D$ -6 (*c* 1.29, $CHCl_3$). Lit.[14b,37] $[\alpha]_D$ -11.6 (*c* 1.5, $CHCl_3$). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm: 170.4-169.3 (4 O$\underline{C}$OCH$_3$), 101.4 (C-1), 71.0 (C-3), 70.6 (C-5), 70.3 (C-1'), 69.0 (C-2), 67.1 (C-4), 61.3 (C-6), 31.9, 29.6, 29.4, 26.1, 22.7 (CH_2 alkyl chain), 20.7 (4 OCO$\underline{C}$H$_3$), 14.1 (CH_3 alkyl chain).

Decyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**17α**) and its β-anomer (**17β**) were obtained in ratio 73/4 (1.88 g, 77% overall yield).

Data for **17α**: $[\alpha]_D$ +42 (*c* 1.56, $CHCl_3$). Lit.[14b] $[\alpha]_D$ +37.8 (*c* 1, CH_2Cl_2). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm: 170.6-169.7 (4 O$\underline{C}$OCH$_3$), 97.6 (C-1), 69.7 (C-2), 69.2 (C-3), 68.5 (C-1'), 68.4 (C-5), 66.3 (C-4), 62.5 (C-6), 31.9, 29.5, 29.3, 26.1, 22.7 (CH_2 alkyl chain), 20.7 (OCO$\underline{C}$H$_3$), 14.1 (C-10', CH_3 alkyl chain).

Data for **17β**: $[\alpha]_D$ -30 (*c* 1.76, $CHCl_3$). Lit.[14b] $[\alpha]_D$ -27.6 (*c* 1, CH_2Cl_2). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm: 170.7-169.6 (4 O$\underline{C}$OCH$_3$), 98.8 (C-1), 72.4 (C-5), 71.3 (C-3), 70.5 (C-1'), 68.9 (C-2), 66.3 (C-4), 62.7 (C-6), 31.9, 29.6, 29.4, 26.1, 22.7 (CH_2 alkyl chain), 20.7 (OCO$\underline{C}$H$_3$), 14.2 (C-10', CH_3 alkyl chain).

Saponification of 9α, 13α, 17α. As described for glucopyranoside **4**, compounds **10α, 14α, 18α** were obtained from **9α, 13α, 17α** respectively in 4 min under microwave irradiation (P: 40-20 W, final *T*: 100-115 °C) in quantitative yields.

Data for **10α**: ^{13}C NMR (75.5 MHz, CD_3OD) δ ppm: 100.7 (C-1), 76.1 (C-5), 74.2 (NH-CO-O<u>C</u>H_2CCl_3), 71.8 (C-3), 68.9 (C-1'), 62.9 (C-4), 62.3 (C-6), 57.4 (C-2), 33.8, 33.0, 30.7, 30.4, 27.4, 24.5, 23.7 (CH_2 alkyl chain), 14.5 (C-10' CH_3 alkyl chain).

Data for **14α**: ^{13}C NMR (62.9 MHz, CD_3OD) δ ppm: 100.3 (C-1), 72.3 (C-5*), 71.6 (C-3*), 71.1 (C-2*), 70.3 (C-4), 69.2 (C-1'), 62.7 (C-6), 33.7, 33.0, 30.7, 30.4, 27.3, 24.5, 23.7 (CH_2 alkyl chain), 14.4 (C-10' CH_3 alkyl chain).

Data for **18α**: ^{13}C NMR (50.3 MHz, CD_3OD) δ ppm: 101.7 (C-1), 74.5 (C-5), 72.4 (C-3*), 72.1 (C-2*), 68.7 (C-1'), 67.6 (C-4), 61.3 (C-6), 33.0, 30.7, 30.5, 27.3, 24.4, 23.7 (CH_2 alkyl chain), 14.5 (C-10' CH_3 alkyl chain).

* Interchangeable assignments.

ACKNOWLEDGEMENTS

This work was supported by the "Direction Générale de l'Alimentation", Ministère de l'Agriculture et de la Pêche. Appreciation is extended to Prolabo company for the donation of the equipment used to carry out this investigation.

REFERENCES AND NOTES

1. A. J. J. Straathof, H. van Bekkum and A. P. G. Kieboom, *Starch*, **40**, 229 (1988).
2. T. Mukaiyama, K. Matsubara and M. Hora, *Synthesis*, 1368 (1994).
3. G. R. Ames, *Chem. Rev.*, **60**, 541 (1960).
4. B. Havlinova, M. Kosik, P. Kovak and A Blazej, *Tenside Detergents*, **14**, 72 (1978).
5. R. F. D. Jones, P. Camilleri, A. J. Kirby and G. N. Okafo, *J. Chem. Soc., Chem. Commun.*, 1311 (1994).
6. M. Biermann, K. Hill, W. Wust, R. Eskuchen, J. Wollmann, A. Buns, G. Hellmann, K. H. Ott, W. Winkle and K. Wollmann, *Eur. Pat.*, 0 301 298, 1988.
7. V. Ferrières, J. N. Bertho and D. Plusquellec, *Tetrahedron Lett.*, **36**, 2749 (1995).
8. A. T. J. W. de Goede, M. P. J. van Deurzen, I. G. van der Leij, A. M. van der Heijden, J. M. A. Baas, F. van Rantwijk and H. van Bekkum, *J. Carbohydr. Chem.*, **14**, 331 (1996).
9. V. Huchel, C. Schmidt and R. R. Schmidt, *Tetrahedron Lett.*, **36**, 9457 (1995).
10. R. R. Schmidt, *Angew. Chem. Int. Ed. Engl.*, **25**, 212 (1986).
11. K. Toshima and K. Tatsuta, *Chem. Rev.*, **83**, 1503 (1993).
12. H. Bertsch and G. Rauchalles, *U. S. Pat.*, 2 049 758, 1936.
13. C. R. Noller and W. C. Rockwell, *J. Am. Chem. Soc.*,**60**, 2076 (1938); W. W. Pigman and N. K. Richtmyer, *J. Am. Chem. Soc.*,**64**, 369 (1942).
14. a) W. Klotz and R. R. Schmidt, *Liebigs Ann. Chem.*, 683 (1993).
    b) W. Klotz and R. R. Schmidt, *J. Carbohydr. Chem.*, **12**, 1093 (1994).

15. A. Loupy, *Spectra Analyse*, **165**, 33 (1993).
16. C. R. Strauss and R. W. Trainor, *Aust. J. Chem.*, **47**, 1665 (1995).
17. S. Caddick, *Tetrahedron*, **51**, 10403 (1995).
18. D. Stuerga and P. Gaillard, *Tetrahedron*, **52**, 5505 (1996).
19. D. A. Lewis, J. D. Summers, T. C. Ward and J. E. Mc Grath, *J. Polym. Science, Part A*, **30**, 1647 (1992).
20. a) A. Morcuende, S. Valverde and B. Herradon, *Synlett*, 89 (1994). b) B. Herradon, A. Morcuende and S. Valverde, *Synlett*, 455 (1995).
21. L. H. B. Baptistella, A. Z. Neto, H. Onaga and E. A. M. Godoi, *Tetrahedron Lett.*, **34**, 8407 (1993).
22. S. Sowmya and K. K. Balasubramanian, *Synth. Commun.*, **24**, 2097 (1994).
23. A. J. J. Straathof, H. van Bekkum and A. P. G. Kieboom, *Recl. Trav. Chim. Pays Bas*, **97**, 647 (1988).
24. M. Csiba, J. Cléophax, A. Loupy, J. Malthête and S. D. Gero, *Tetrahedron Lett.*, **34**, 1787 (1993).
25. M. Majdoub, A. Loupy, A. Petit and S. Roudesli, *Tetrahedron*, **52**, 617 (1996).
26. Hyflo Super Cel composition according to Fluka informations: silica 89.3%; Al_2O_3 4.2%; Na_2O,K_2O 3.5%; Fe_2O_3 1.4%. Silica structures are a mixture of α-cristobalite and α-tridymite. Particles size : 2-25 μ.
27. J. R. Carrillo-Munoz, D. Bouvet, E. Guibé-Jampel, A. Loupy and A. Petit, *J. Org. Chem.* (1996), in press.
28. a) A. Trincone, R. Improta and A. Gambacorta, *Biocatalysis and Biotransformation*, **11**, 77 (1995). b) G. Vic and D. H. G. Crout, *Tetrahedron Asymmetry*, **5**, 2513 (1994). c) K. Ajisaka, H. Nishida and H. Fujimoto, *Biotechnol. Lett.*, **8**, 387 (1987).
29. R. U. Lemieux and A. R. Morgan, *Can. J. Chem.*, **43**, 2205 (1965).
30. R. S. Varma, M. Varma and A. K. Chatterjee, *J. Chem. Soc. Perkin Trans. I* , 999 (1993).
31. a) K. Higashi and H. Susaki, *Chem. Pharm. Bull.*, **40**, 2019 (1992). b) K. Higashi, K. Nakayama, K. Uoto, E. Shioya and T. Kusama, *Chem. Pharm. Bull.*, **38**, 590 (1991). c) K. Higashi, K. Nakayama, T. Soga, K. Uoto, E. Shioya and T. Kusama, *Chem. Pharm. Bull.*, **37**, 3280 (1990).
32. J. Inanaga, Y. Yokoyama and T. Hanamoto, *Tetrahedron Lett.*, **34**, 2791 (1993).
33. a) A. Loupy, P. Pigeon and M. Ramdani, *Tetrahedron*, **52**, 6705 (1996). b) A. Diaz-Ortiz, P. Prieto, A. Loupy and D. Abenhaïm, *Tetrahedron Lett.*, **37**, 1695 (1996).
34. K. D. Raner, C. R. Strauss, F. Vyskoc and L. Mokbel, *J. Org. Chem.*, **57**, 950 (1993).
35. a) K. Bougrin, A. K. Bennani, S. F. Tétouani and M. Soufiaoui, *Tetrahedron Lett.*, **35**, 8373 (1994). b) A. Chandra Sheker Reddy, P. Shanthan Rao and R. V. Venkataratnam, *Tetrahedron Lett.*, **37**, 2845 (1996). c) A. Loupy, P. Pigeon, M. Ramdani and P. Jacquault, *Synth. Commun.*, **24**, 159 (1994). d) D. A. Lewis, *Mat. Res. Soc. Symp. Proc.*, **268**, 21 (1992).
36. P. Jacquault, *Eur. Pat.*, 92 420477, 1992.
37. a) R. Hori and Y Ikegami, *Yakugaku Zasshi*, **78**, 80 (1959); C. A., **53**, 10049g (1959). b) H. H. Young, *U. S. Pat.*, 2 422 328, 1947; C. A., **41**, 5753 (1947).