Available online at www.sciencedirect.com
SCIENCE DIRECT®
Carbohydrate Research 339 (2004) 2821–2833
Carbohydrate RESEARCH

Synthesis of *N*-unsubstituted, mono- and disubstituted carbohydrate-1-*O*-carbamates and their behaviour in glycoside syntheses

Hans-Peter Knoben, Urs Schlüter and Hartmut Redlich*

Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster, Corrensstraße 40, 48149 Münster, Germany

Received 26 August 2004; accepted 3 October 2004
Available online 28 October 2004

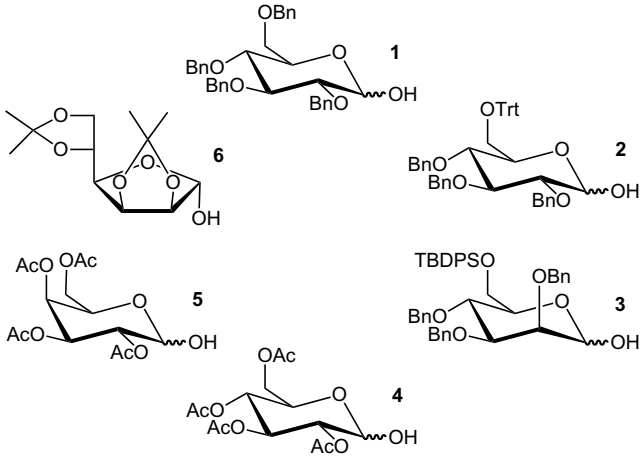
Abstract—The syntheses of 44 1-carbamates from six different 1-*O*-unprotected carbohydrate derivatives (compounds **1**–**6**), representing typical protecting pattern in glycoside synthesis, are described. The carbamate function is *N*-unsubstituted (compounds **1b**–**6b**), mono- (compounds **a**: *N*-trichloroacetyl, **c**: *N*-monochloroacetyl, **d**: *N*-acetyl, **e**: *N*-ethyl, **f**: *N*-allyl, **g**: *N*-phenyl) or disubstituted (compounds **h**: imidazolyl, **i**: *N*-diethyl, **j**: *N*-diphenyl). Additionally, three *N*-chlorosulfonyl carbamates are synthesized and used as intermediates for the synthesis of *N*-unsubstituted compounds **b**. The accessibility of these compounds is described and compared. Some of the carbamates (**1**, **4**, **5a**–**j**) are used as model compounds for systematic investigations in glycoside syntheses. Selected experimental data (reaction conditions, anomeric ratios, rotation values, selected NMR data) are tabulated.

Keywords: Glycosyl carbamates; Carbohydrate-1-carbamates; Glycosidation; Disaccharides; One-pot reaction

1. Introduction

The carbamate function has been used mainly as a base-labile protecting group for hydroxy functions in carbohydrate chemistry. The varying reactivity of hydroxy groups on the one hand and the reactivity of the isocyanates, influenced by its substituents, on the other hand offered a variety of suitable solutions.[1] In 1993 Kunz and Zimmer[2] reported the synthesis of carbohydrate-1-(*N*-allyl)-carbamates and their use in glycoside synthesis. Hinklin and Kiessling[3] used glycosyl sulfonylcarbamates as glycosyl donors. They also achieved a tuning in reactivity of the donors by using different residues in the carbamate function. Other authors have worked on further aspects of 1-*O*-glycosyl carbamates.[4]

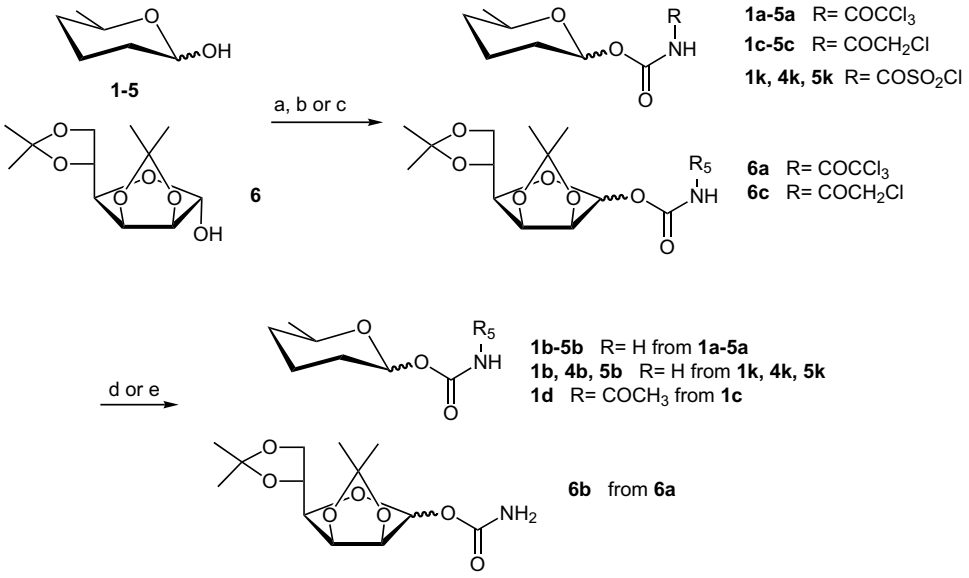
The studies reported here deal with the synthesis of carbohydrate-1-carbamates and their behaviour in glycoside syntheses. As it will be shown some of the synthesized carbamates posses good properties as glycosyl donors. For the following studies six anomerically unprotected carbohydrate derivatives (Scheme 1) were used. They are typical representatives in the area of glycoside synthesis with regard to their configuration and



Scheme 1.

* Corresponding author. E-mail: redlich@uni-muenster.de

0008-6215/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2004.10.002



Scheme 2. Reagents and conditions: (a) Cl_3Ac–NCO, CH_2Cl_2, rt, 1 min, quant.; (b) ClO_2S–NCO, CH_2Cl_2, rt, 1 min, quant.; (c) ClAc–NCO, CH_2Cl_2, rt, 1 min, quant.; (d) column chromatography on silica gel or Al_2O_3; (e) Zn, AcOH, 30–40 °C, 24 h, quant.

protection groups. The syntheses were carried out according to known procedures in the literature.[5]

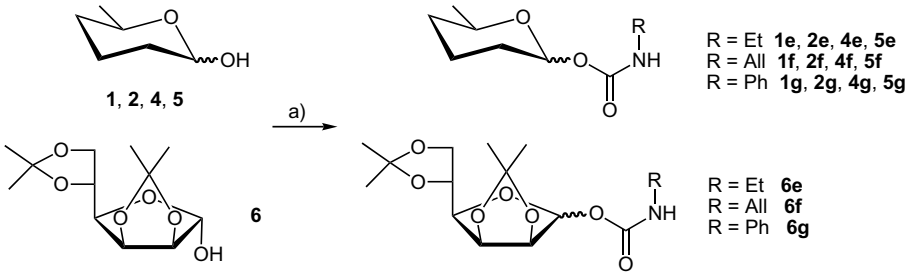
2. Results and discussion

2.1. Synthesis of carbamates 1(a–j)–6(a–j)

The preparations of the *N*-acyl-1-*O*-glycosyl carbamates were carried out by direct reaction of chlorosulfonyl-, trichloroacetyl or monochloroacetyl isocyanates with the anomeric unprotected carbohydrate derivatives (**1**–**6**). These carbohydrate compounds reacted with commercially available *N*-acyl isocyanates—considered as typical representatives of the more reactive isocyanates—in dry dichloromethane at room temperature within a minute (Schemes 2 and 3). The resulting *N*-acyl-1-*O*-glycosyl carbamates (**1a**,**c**,**d**, **2a**,**c**, **3a**, **4a**,**c**, **5a**,**c**, **6a**,**c**) were usually obtained in quantitative yield (Scheme 2).

As shown in Scheme 2 (procedure d or e) the *N*-acyl-1-*O*-glycosyl carbamates differed in their hydrolysis sensitivity: the chlorosulfonyl-substituted carbamates (**1k, 4k, 5k**) could not be isolated in pure form as they underwent a rapid hydrolysis followed by decomposition. A fast filtration of the reaction mixture over silica gel or neutral aluminium oxide lead, however, to the controlled splitting-off of the acyl residues. The isolation of the corresponding *N*-unsubstituted 1-carbamates (**1b**, **4b**, **5b**) was successful in high yields with carbohydrate compounds carrying more acid-stable (e.g., benzyl ether groups) protecting groups.

The trichloroacetyl-substituted carbamates (**1a**, **2a**, **3a**, **4a**, **5a**, **6a**) were recognizably more stable and could be isolated in pure form and therefore favourable starting compounds for the synthesis of the stable *N*-unsubstituted carbamates (**1b**, **2b**, **3b**, **4b**, **5b**, **6b**). As expected, the monochloroacetyl derivatives (**1c**, **2c**, **3c**, **4c**, **5c**, **6c**) were the most stable of the group of compounds in question here. They did not undergo hydrolysis reactions on



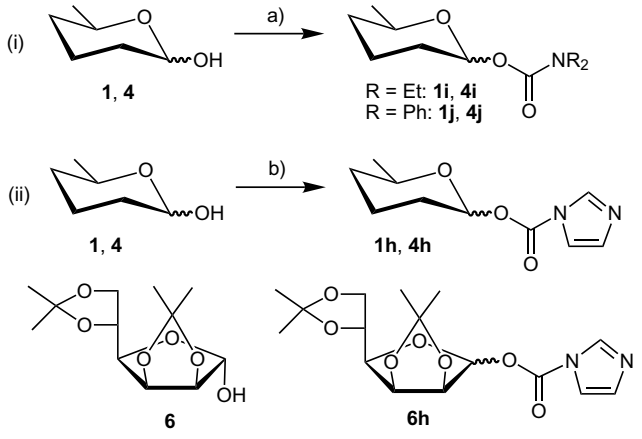
Scheme 3. Reagents and conditions: (a) NaH, R-NCO, CH_2Cl_2, rt, 20–40 min; R = Et, All, Ph.

silica gel or neutral aluminium oxide and therefore could be isolated and handled easily. The monochloroacetyl carbamates were easily dehydrohalogenated to the corresponding acetyl carbamates (**1d**) with zinc and glacial acetic acid (Scheme 2e). All carbamates obtained from these reactions were anomeric mixtures. Because of the good stability of the unsubstituted or the monochloroacetyl-substituted carbamates, a chromatographic separation into the pure anomers was possible (see Section 4), so that these could be examined as anomerically pure compounds.

N-Alkyl and *N*-aryl isocyanates were less reactive than the acyl derivatives discussed above, therefore the anomeric alcohol had to be activated. Good results were achieved with different *N*-bases (e.g., pyridine, alkyl substituted amines, etc.). In this study, the required activation was carried out exclusively by sodium hydride[6] since this brought advantages with respect to handling and yield. To avoid the formation of allophanates, it was necessary to work with stoichiometric ratios.[7] The synthesis of the *N*-ethyl (**1e**, **2e**, **4e**, **5e**, **6e**), *N*-allyl (**1f**, **2f**, **4f**, **5f**, **6f**) or *N*-phenyl (**1g**, **2g**, **4g**, **5g**, **6g**) substituted carbamates was simple and the products were obtained in high yields (Scheme 3).

Some *N*-disubstituted carbamates (**1i**,**j**, **4i**,**j**) were obtained from the reaction of *N*-diethyl or *N*-diphenyl carbamoylchloride and the corresponding anomeric unprotected carbohydrate derivatives **1** and **4** in pyridine (Scheme 4i). In comparison with the methods described above this procedure, however, was not very efficient. A relative large excess of the carbamoylchlorides, higher temperatures and longer reaction times were necessary to get sufficient results (60–90% yields).

The preparation of the carbonylimidazolyl compounds (**1h**, **4h**, **6h**) differed due to their chemical behaviour as azolides.[8] The syntheses were carried out by



Scheme 4. Reagents and conditions: (a) dialkyl carbamoyl chloride, pyridine, 80 °C, 48 h, R = Et or Ph; (b) *N*,*N*′-carbonyldiimidazole, Et_2O, reflux, 4 h.

treating compounds **1**, **4** or **6** with an excess of *N*,*N*′-carbonyldiimidazole in refluxing ether. Within 4 h 90–100% yields are obtained (Scheme 4ii).

2.2. Glycosidation reactions

The structural similarity of the carbamate function to the leaving group of the glycosyl donors in Schmidt's trichloroacetimidate method[9] suggests an activation for glycosylation reactions via 'hard' Lewis acids. Activating the anomeric carbamate function in a glycoside synthesis is possible in two different ways: the attack of the promoter can occur either at the anomeric or at the carbonyl oxygen.

Ford and Ley[10] pointed out for the first time, that a basic difference exists for the activation of carbohydrate-1-carbonyl- or carbohydrate-1-thiocarbonylimidazolides. While the former are activated excellently with the very 'hard'[11] zinc dibromide the corresponding thio compounds are activated more easily by 'soft' silver perchlorate. This suggests that in the latter case the activation is operating via the sulfur of the thiocarbonyl group, in other words, a 'remote activation'[12] of the anomeric centre takes place.

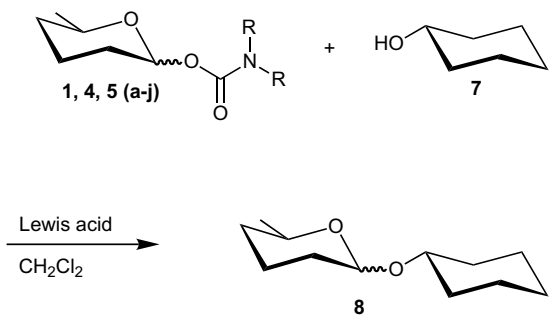
Using anomeric *N*-allyl carbamates, Kunz and Zimmer[2] suggests the anomeric activation at an even further remote position of the glycosyl donor. These carbamates can be activated very well with 'soft' classified iodonium-ion supplying promoters. The authors consider a mechanistic analogy for *N*-allyl carbamates to the established pentenyl method of Fraser-Reid et al.,[13] in which the primary activation is carried out at the double bond of the pentenyl group.

In the following the behaviour of unsubstituted carbohydrate-1-carbamates were examined. Their possible activation cannot be influenced by further substituents at the carbamate function. In addition, several substituted carbohydrate-1-carbamates are examined regarding the inductive and/or mesomeric influence of substituents at the *N*-atom of the carbamate function.

Ten different Lewis acids [$SnCl_4$, $AlCl_3$, anhyd $FeCl_3$, $BF_3{\cdot}OEt_2$, $TrtClO_4$, MeOTf, TMSOTf, $ZnCl_2$, $Cu(OTf)_2$, $Sn(OTf)_2$] classified from very 'hard' to moderate, were examined as the promoter in glycosidation reactions. To receive an impression about the influence of the different Lewis acids and the possibilities of activating different type of carbamates, the anomeric carbamates **1a**–**j** were reacted with the reactive secondary alcohol cyclohexanol **7** (Scheme 5).

Table 1 summarizes these examinations. The particular reaction times and the anomeric ratio of the resulting cyclohexyl glycoside (NMR-spectroscopically determined) are also tabulated.

As these experiments show there was not a single carbamate function, which could not be activated for a glycosidation reaction and there was not one promoter in



Scheme 5.

the list, which did not activate at least one of the carbamate functions.

The bivalent ions of the metals zinc, copper and tin showed the poorest results. All other examined promoters usually activated several differently substituted carbamate functions, partly with recognizable preferences (Table 1). The average yields for the 10 promoters applied to the 10 different leaving groups vary from 0.8% ($Cu(OTf)_2$ to 72.8% ($SnCl_4$) contrast, the average yield for one single leaving group with the 10 different promoters varied only from 17.5% (**1i**) to 36.7% (**1b**) (Table 1, horizontal entry).

In general the use of tin tetrachloride (average yield with the 10 different carbamates 72.8%) and trimethylsilyl triflate (average yield with the 10 different carbamates 49.1%) gave good conversion, particularly considering the 1/1.1 ratio of the components. Both promoters induced the glycoside synthesis in dichloromethane at room temperature within a few minutes. Therefore the reactivity of the system anomeric carbamate/tin tetrachloride or trimethylsilyl triflate is high.

The NMR-spectroscopic determined anomeric ratios listed in Table 1 should not be overvalued for the Lewis acids. The reactivity of both the donor (1-*O*-carbamate/promoter) and the acceptor (cyclohexanol with a secondary hydroxy function), are both high. Consequently a distinctive selectivity is hard to expect for these model reactions.

Two characteristic representatives of glycosyl acceptors, which may occur in more complex oligo- or polysaccharide syntheses were also examined: a very reactive carbohydrate alcohol, methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **9**, with a primary hydroxy function and a rather unreactive carbohydrate alcohol, methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside **13**, with a secondary hydroxy function, were used as models for glycosyl acceptors. Both are easily available by well established literature procedures.[14,15] By using these acceptors the determination of the anomeric ratio in the resulting disaccharides is simple. The mixtures are usually not separated by chromatographic methods and so yields are estimated by integration of the characteristic methyl glycoside ^{1}H NMR signals in the crude reaction mixture.

The formation of the (1→6)-disaccharides **10**–**12** was carried out using the reaction conditions found before (Scheme 6).

Usually these reactions resulted in very good to excellent yields and were finished in 30 min for the more reactive glycosyl carbamates **1a**–**d**, (Table 2, entries 1–6). The other glycosyl carbamates needed a few hours (Table 2, entries 7–30). It is noteworthy that some stereoselectivity occurred when benzyl protected anomerically pure glycosyl donors were used: The two stable and separable *N*-acetyl carbamates (**1c** and **1d**) gave a slight excess of either the α-disaccharide **10**α starting from the β-*N*-acetyl carbamates (**1c**β and **1d**β) or the β-disaccharide **10**β starting from the α-*N*-acetyl carbamates, **1c**α and **1d**α, (Table 2, entries 3–6).

The glycosyl carbamates (**4a**–**c**,**e**–**j**, **5a**–**c**,**e**–**g**) carrying participating neighbouring groups at C-2 reacted with complete stereoselective formation of β-1,2-*trans*-glycosides (**11**, **12**) as already expected from Isbell perception more than 60 years ago,[16] that a participating group, when present at O-2 of the glycosyl donor, promotes 1,2-*trans* selectivity.[17]

Basically, the glycosidations using the more unreactive glycosyl acceptor methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (**13**) (Scheme 7) were carried out using the same protocol described above.

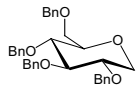
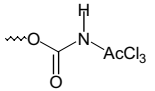
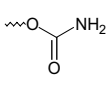
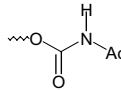
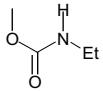
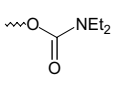
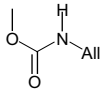
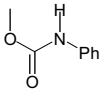
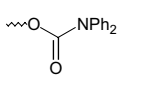
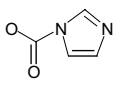
The results were comparable regarding to yields and reaction time in spite of the lower reactivity of the acceptor (Table 3).

The formation of methyl 4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α,β-D-glucopyranoside (**14**) in a 70% yield from 2,3,4,6-tetra-*O*-benzyl-1-*O*-*N*-chloroacetyl-carbamoyl)-α-D-glucopyranose (**1c**α) within 30 min with a selectivity of 6.0:1 for the β-product (Table 3, entry 3) is remarkable. The corresponding β-donor **1c**β yielded within 30 min in 69% with a 3.0:1 anomeric selectivity in favour for the α-anomer **14**α (Table 3, entry 4). The same tendency was observed for the α-*N*-acetyl carbamate **1d**α with its 5.0:1 β-selectivity (Table 3, entry 5). Appropriate to this, disaccharide **14**α was obtained from the β-*N*-acetyl carbamate **1d**β with a α-selectivity of 3.0:1 in 65% yield (Table 3, entry 6). This results indicate, that for the less reactive acceptors the selectivity, already observed before, is now much more improved with the most valuable tendency, that α-glycosyl donor will result predominantly in a β-configurated disaccharide and vice versa even under nonoptimized conditions.

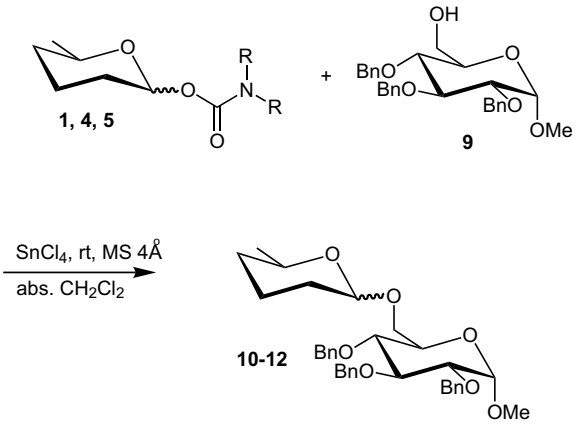
Again, the glycosyl carbamates (**4a**–**c**,**e**–**j**, **5a**–**c**,**e**–**g**) with participating neighbouring groups at C-2 reacted with stereospecific formation of β-1,2-*trans*-glycosides **15** and **16**.

As indicated in Table 3, one-pot applications were easily carried out starting from the anomeric unpro-

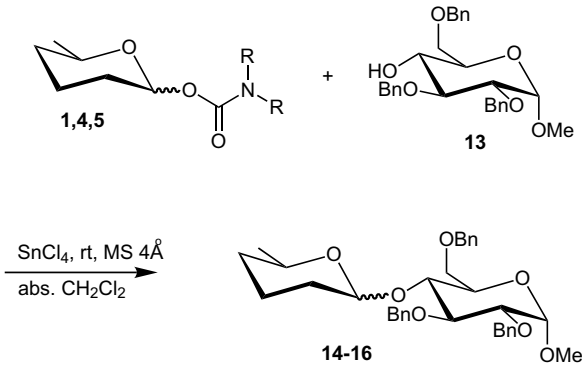
Table 1. Conditions and activities of the promoters for cyclohexyl glycoside **8** formation in CH_2Cl_2 at room temperature

										Average yield (%) [10 carbamates]
	1aα:β = 2:1	**1b**α:β = 2:1	**1c**α	**1d**α	**1e**α	**1i**α:β = 1:1	**1f**α	**1g**α	**1j**α:β = 1:1	**1h**α:β = 3:1	
$SnCl_4$	[a]: **77%** [b]: 1:2 [c]: 30 min	[a]: **75%** [b]: 2:1 [c]: 30 min	[a]: **79%** [b]: 1:3 [c]: 30 min	[a]: **78%** [b]: 1:3 [c]: 30 min	[a]: **67%** [b]: 1.3:1 [c]: 3 h	[a]: **67%** [b]: 1.3:1 [c]: 3 h	[a]: **97%** [b]: 1:1 [c]: 30 min	[a]: **77%** [b]: 1.2:1 [c]: 3 h	[a]: **52%** [b]: 8:1 [c]: 6 h	[a]: **59%** [b]: 2:1 [c]: 5 h	72.8
$AlCl_3$	[a]: **37%** [b]: 1:1.7 [c]: 7 h	[a]: **49%** [b]: 2:1 [c]: 3.5 h	[a]: **35%** [b]: 1:3 [c]: 5 h	[a]: **37%** [b]: 1:2 [c]: 5 h	[a]: **21%** [b]: 2:1 [c]: 24 h	[a]: **18%** [b]: 1:1.5 [c]: 24 h	[a]: **79%** [b]: 2:1 [c]: 24 h	[a]: **77%** [b]: 2:1 [c]: 24 h	[a]: **26%** [b]: 2:1 [c]: 24 h	[a]: **17%** [b]: 2:1 [c]: 15 h	39.6
$FeCl_3$	[a]: **39%** [b]: 1:1.5 [c]: 4 h	[a]: **41%** [b]: 1.9:1 [c]: 4 h	[a]: **34 %** [b]: 1:2 [c]: 5 h	[a]: **35%** [b]: 1:2 [c]: 5 h	[a]: **23%** [b]: 2:1 [c]: 24 h	[a]: — [b]: — [c]: 24 h	[a]: **20%** [b]: 2:1 [c]: 24 h	[a]: **18%** [b]: 2:1 [c]: 24 h	[a]: **38%** [b]: 1.5:1 [c]: 24 h	[a]: **75%** [b]: 2:1 [c]: 24 h	32.3
$BF_3{\cdot}OEt_2$	[a]: **41%** [b]: 1:2 [c]: 3 h	[a]: **32%** [b]: 2:1 [c]: 4 h	[a]: **30%** [b]: 1:2.5 [c]: 5 h	[a]: **34%** [b]: 1:2 [c]: 5 h	[a]: **27%** [b]: 2:1 [c]: 24 h	[a]: **26%** [b]: 1:1.2 [c]: 24 h	[a]: **79%** [b]: 2:1 [c]: 24 h	[a]: **77%** [b]: 2:1 [c]: 24 h	[a]: **16%** [b]: 2:1 [c]: 24 h	[a]: **11 %** [b]: 2:1 [c]: 24 h	37.3
$TrtClO_4$	[a]: **42%** [b]: 1:1.1 [c]: 2 h	[a]: **34%** [b]: 1.3:1 [c]: 2h	[a]: **32 %** [b]: 1:1.3 [c]: 3 h	[a]: **34%** [b]: 1:1 [c]: 3 h	[a]: **20%** [b]: 2:1 [c]: 24 h	[a]: — [b]: — [c]: 24 h	[a]: **22%** [b]: 2:1 [c]: 24 h	[a]: **14%** [b]: 2:1 [c]: 24 h	[a]: — [b]: — [c]: 24 h	[a]: **75%** [b]: 2:1 [c]: 15 h	27.3
MeOTf	[a]: — [b]: — [c]: 48 h	[a]: **42%** [b]: 1:1 [c]: 48 h	[a]: — [b]: — [c]: 48 h	[a]: — [b]: — [c]: 48 h	[a]: — [b]: — [c]: 48 h	[a]: **32%** [b]: 1:1.1 [c]: 24 h	[a]: — [b]: — [c]: 48 h	[a]: — [b]: — [c]: 48 h	[a]: **12%** [b]: 1.4:1 [c]: 24 h	[a]: **20%** [b]: 1:1 [c]: 48 h	10.6
TMSOTf	[a]: **46%** [b]: 1:1.3 [c]: 30 min	[a]: **65%** [b]: 2:1 [c]: 1 h	[a]: **59%** [b]: 1:1.5 [c]: 2 h	[a]: **55%** [b]: 1:1.5 [c]: 2 h	[a]: **42%** [b]: 1.2:1 [c]: 5 h	[a]: **19%** [b]: 1:1.2 [c]: 24 h	[a]: **45%** [b]: 1.4:1 [c]: 5 h	[a]: **39%** [b]: 2:1 [c]: 5 h	[a]: **80%** [b]: 2:1 [c]: 4 h	[a]: **41%** [b]: 2:1 [c]: 5 h	49.1
$ZnCl_2$	[a]: — [b]: — [c]: 24 h	[a]: **29%** [b]: 1.8:1 [c]: 10 h	[a]: — [b]: — [c]: 24 h	[a]: — [b]: — [c]: 24 h	[a]: — [b]: — [c]: 24 h	[a]: — [b]: — [c]: 24 h	[a]: — [b]: — [c]: 24 h	[a]: — [b]: — [c]: 24 h	[a]: — [b]: — [c]: 24 h	[a]: — [b]: — [c]: 10 h	29.0
$Cu(OTf)_2$	[a]: — [b]: — [c]: 15 h	[a]: — [b]: — [c]: 15 h	[a]: — [b]: — [c]: 15 h	[a]: — [b]: — [c]: 15 h	[a]: — [b]: — [c]: 15 h	[a]: — [b]: — [c]: 24 h	[a]: — [b]: — [c]: 15 h	[a]: — [b]: — [c]: 15 h	[a]: **8%** [b]: 1:1 [c]: 24 h	[a]: — [b]: — [c]: 15 h	0.8
$Sn(OTf)_2$	[a]: — [b]: — [c]: 15 h	[a]: — [b]: — [c]: 15 h	[a]: — [b]: — [c]: 15 h	[a]: — [b]: — [c]: 15 h	[a]: — [b]: — [c]: 15 h	[a]: **13%** [b]: 1:1 [c]: 15 h	[a]: — [b]: — [c]: 15 h	[a]: — [b]: — [c]: 15 h	[a]: **45%** [b]: 1:1 [c]: 24 h	[a]: — [b]: — [c]: 15 h	5.8
Average yield (%) [10 catalysts]	28.2	36.7	26.9	27.3	20.0	17.5	34.2	30.2	27.7	29.8	

[a]: Yield of isolated cyclohexyl glycoside **8**; [b]: anomeric ratio (α:β); [c]: reaction time, reaction was finished when no educt can be detected by TLC-analysis or when no reaction took place.



Scheme 6.



Scheme 7.

Table 2. Glycosidation reactions of selected carbamates with methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **9** as a glycosyl acceptor, $SnCl_4$ and CH_2Cl_2

Entry	Glycosyl donor	Time	Product	Yield (%)	α:β	Remarks
1	**1a**αβ 2:1	30 min	**10**	92	1:2.0	1
2	**1b**αβ 2:1	30 min	**10**	82	2.2:1	
3	**1c**α	30 min	**10**	91	1:2.0	2
4	**1c**β	30 min	**10**	86	2.0:1	2
5	**1d**α	30 min	**10**	90	1:2.0	
6	**1d**β	30 min	**10**	87	2.0:1	
7	**1e**α	3 h	**10**	57	1.4:1	
8	**1f**α	3 h	**10**	70	1.0:1	
9	**1f**α	12 h	**10**	92	1.0:1	
10	**1g**α	3 h	**10**	72	1.1:1	
11	**1h**αβ 3:1	2 h	**10**	61	2.0:1	
12	**1i**αβ 1:1	24 h	**10**	24	1.0:1	
13	**1j**αβ 1:1	24 h	**10**	21	1.0:1	
14	**4a**αβ 1:3	2 h	**11**	88	Only β	1
15	**4b**αβ 1:3	30 min	**11**	88	Only β	
16	**4c**α	2 h	**11**	83	Only β	2
17	**4c**β	2 h	**11**	85	Only β	2
18	**4e**β	6 h	**11**	57	Only β	
19	**4f**αβ 1:3	2 h	**11**	88	Only β	
20	**4g**β	6 h	**11**	51	Only β	
21	**4h**αβ 1:3	4 h	**11**	50	Only β	
22	**4i**αβ 1:1	24 h	**11**	9	1:4.0	
23	**4j**β 1:1	24 h	**11**	14	1:1.5	
24	**5a**αβ 1:4	3 h	**12**	85	Only β	1
25	**5b**αβ 1:4	1 h	**12**	81	Only β	
26	**5c**α	2 h	**12**	80	Only β	2
27	**5c**β	2 h	**12**	75	Only β	2
28	**5e**β	6 h	**12**	73	Only β	
29	**5f**αβ 1:3	2 h	**12**	82	Only β	
30	**5g**β	6 h	**12**	70	Only β	

1: One-pot procedure; 2: separated anomers, one-pot procedure possible.

Table 3. Glycosidation reactions of selected carbamates with methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside **13** as a glycosyl acceptor, $SnCl_4$ and CH_2Cl_2

Entry	Glycosyl donor	Time	Product	Yield (%)	α:β	Remarks
1	**1a**αβ 2:1	30 min	**14**	71	1:3.0	1
2	**1b**αβ 2:1	30 min	**14**	65	2.0:1	
3	**1c**α	30 min	**14**	70	1:6.0	2
4	**1c**β	30 min	**14**	69	3.0:1	2
5	**1d**α	30 min	**14**	72	1:5.0	
6	**1d**β	30 min	**14**	65	3.0:1	
7	**1e**α	5 h	**14**	43	1.1:1	
8	**1f**α	4 h	**14**	46	1.0:1	
9	**1f**α	17 h	**14**	76	3.0:1	
10	**1g**α	7 h	**14**	49	1.2:1	
11	**1h**αβ 3:1	2 h	**14**	42	2.0:1	
12	**1i**αβ 1:1	24 h	**14**	8	1.0:1	
13	**1j**αβ 1:1	24 h	**14**	12	1.0:1	
14	**4a**αβ 1:3	2 h	**15**	47	Only β	1
15	**4b**αβ 1:3	3 h	**15**	51	Only β	
16	**4c**α	3 h	**15**	51	Only β	2
17	**4c**β	3 h	**15**	47	Only β	2
18	**4e**β	7 h	**15**	31	Only β	
19	**4f**αβ 1:3	6 h	**15**	49	Only β	
20	**4g**β	7 h	**15**	41	Only β	
21	**4h**αβ 1:3	4 h	**15**	33	Only β	
22	**4i**αβ 1:1	24 h	—	—	—	No reaction
23	**4j**αβ 1:1	24 h	**15**		1:0.8	
24	**5a**αβ 1:4	3 h	**16**	40	Only β	1
25	**5b**αβ 1:4	3.5 h	**16**	47	Only β	
26	**5c**α	3 h	**16**	39	Only β	2
27	**5c**β	3 h	**16**	42	Only β	2
28	**5e**β	7 h	**16**	33	Only β	
29	**5f**αβ 1:3	3 h	**16**	45	Only β	
30	**5g**β	7 h	**16**	37	Only β	

1: One-pot procedure; 2: separated anomers, one-pot procedure possible.

tected carbohydrate. Applying the equivalent amount of one of the more reactive isocyanates (e.g., trichloro- or monochloroacetyl), the promoter and the hydroxy component resulted in the corresponding glycosides independent of the reactivity of the OH-function.

3. Conclusion

Glycosyl carbamates are most promising glycosyl donors in glycoside syntheses. They can be easily synthesized and isolated as very stable compounds or

generated and applied 'in situ' (one-pot glycosidation procedures). Promoted with $SnCl_4$ in dichloromethane at room temperature, glycosyl carbamates exhibit a pronounced reactivity towards hydroxy functions. The less reactive 4-hydroxy function in compound **13** can be coupled within minutes.

Anomers of glycosyl carbamates with nonparticipating neighbouring group protecting patterns exhibited a pronounced tendency (even in standard conditions) to react in a S_N2-type manner. This would give rise to the opposite configuration in the glycoside, a most valuable finding for further investigations.

4. Experimental

4.1. General methods

All reactions and purification steps were monitored by TLC on silica gel plates (Merck silica gel plates $60F_{254}$). The detection of the compounds was carried out by treating the plates with a 1/1 (v/v) mixture of a solution of naphtoresorcine in ethanol and 2 M sulfuric acid and heating column chromatography up to 5 g scale was carried out by MPLC (medium pressure column chromatography, Pump: ProMinent Duramat, pressure = 3–5 bar) with silica gel 60 (230–400 mesh) from Merck. Column chromatography over 5 g scale was carried out by column chromatography at normal pressure with silica gel 60 (70–400 mesh) from Merck. Melting points were measured with a melting point apparatus from Mettler (type: FP61) and are uncorrected. Optical rotations were measured with a polarimeter 241 or 341 (Perkin–Elmer) in a 1 dm tube (589 nm, Na-D-line, 20 °C, concentration: 10 mg/mL). NMR spectra were measured with a Bruker WM 300 (^{1}H: 300.13 MHz, ^{13}C: 75.48 MHz), a Bruker AM 360 (^{1}H: 360.13 MHz, ^{13}C: 90.56 MHz), a AMX 400 (^{1}H: 400.13 MHz, ^{13}C: 100.62 MHz) or a Varian-spectrometer UNITY*plus* 600 (^{1}H: 599.86 MHz, ^{13}C: 150.85 MHz).

4.2. Method A: Synthesis of *N*-acyl 1-*O*-glycosyl carbamates

The acyl isocyanate or the chlorosulfonyl isocyanate (1.1 mmol) was added to a solution of the corresponding carbohydrate derivative (1 mmol) in absolute dichloromethane.[18] The reaction was complete after 1 min reaction time. The reaction solution was concentrated and in case of *N*-chlorosubstituted acyl 1-*O*-glycosyl carbamates the compound could be purified by column chromatography eluting with a cyclohexane ethyl acetate mixture (exact ratio of the solvents depended mostly on the protecting groups of the carbohydrate, usually a 1:1 mixture was adequate).

4.3. Method B: Synthesis of *N*-unsubstituted 1-*O*-glycosyl carbamates

The chlorosulfonyl carbamates or the trichloroacetyl carbamates were cleaved and purified by column chromatography using ethyl acetate as eluent (Tables 4 and 5).

4.4. Method C: Synthesis of *N*-acetyl 1-*O*-glycosyl carbamates

A small amount of zinc dust was added to a solution of 1 mmol carbamate **1c** in glacial acetic acid at a reaction temperature of 40 °C. When the reaction was complete (TLC-monitoring, exact reaction times are presented in Table 1), the reaction mixture was filtered in order to remove zinc salts. The reaction solution was concentrated. Further purification by column chromatography was not possible due to the products small stability.

4.5. Method D: Synthesis of *N*-monosubstituted 1-*O*-glycosyl carbamates

Sodium hydride (1.3 mmol) was added to a solution of 1 mmol of the carbohydrate in dichloromethane at room temperature. After 1 h 1 mmol of the corresponding isocyanate was added. When the reaction was completed (TLC-monitoring, exact reaction times are presented in Table 1) the reaction mixture was filtered over Celite. The reaction solution was concentrated and could be purified by column chromatography eluting with a cyclohexane ethyl acetate mixture (exact ratio of the solvents depended mostly on the protecting groups of the carbohydrate, usually a 1:1 mixture was adequate).

4.6. Method E: Synthesis of 1-*O*-carbonylimidazolyl glycosides

N,*N*′-Carbonyldiimidazole (10 mmol) was added to a solution of 1 mmol carbohydrate in dry diethylether.[10] The reaction mixture was refluxed until the reaction was complete (TLC-monitoring, exact reaction times are presented in Table 1). The reaction mixture was washed with ammonium chloride solution, dried over sodium sulfate and concentrated. Further purification by column chromatography was not possible due to the products small stability.

4.7. Method F: Synthesis of *N*-disubstituted 1-*O*-glycosyl carbamates

N,*N*′-Dialkyl carbamoylchloride (10.0 mmol) was added to a solution of 1 mmol of carbohydrate in dry pyridine.[10] The reaction mixture was heated to 70 °C until the reaction was complete (TLC-monitoring, exact reaction times are presented in Table 1). The solution was poured

Table 4. Preparation of 1-*O*-glycosyl carbamates

Starting material	Substrate	Product	Method	Time	Yield (%)	α:β
1	Cl_3AcNCO	**1a**	A	1 min	100	2:1
1a		**1b**	B	1 h	92	2:1
1	ClAcNCO	**1c**	A	1 min	100	2:1
1c		**1d**	C	24 h	100	α→α[a] β→β[a]
1	EtNCO	**1e**	D	20 min	94	2:1
1	AllNCO	**1f**	D	20 min	85	10:1
1	PhNCO	**1g**	D	20 min	90	2:1
1	Im_2CO	**1h**	E	4 h	100	2:1
1	$Et_2N(CO)Cl$	**1i**	F	48 h	55	1:3
1	$Ph_2N(CO)Cl$	**1j**	F	48 h	74	1:2
1	$ClSO_2NCO$	**1k**	A	1 min	100	2:1
2	Cl_3AcNCO	**2°**	A	5 min	85	1:1
2a		**2b**	B	1 h	71	1:2
2	ClAcNCO	**2c**	A	90 min	76	1:1
2	EtNCO	**2e**	D	3.5 h	50	1:1
2	AllNCO	**2f**	D	3 h	83	1:1
2	PhNCO	**2g**	D	3 h	84	1:1
3	Cl_3AcNCO	**3a**	A	1 min	100	Only α
3a		**3b**	B	1 h	100	Only α
3	ClAcNCO	**3c**	A	1 min	100	6:1
4	Cl_3AcNCO	**4a**	A	1 min	100	1:3
4a		**4b**	B	1 h	90	1:3
4	ClAcNCO	**4c**	A	1 min	100	1:3
4	EtNCO	**4e**	D	40 min	92	1:3
4	AllNCO	**4f**	D	20 min	81	1:3
4	PhNCO	**4g**	D	40 min	94	1:3
4	Im_2CO	**4h**	E	4 h	100	2:1
4	$Et_2N(CO)Cl$	**4i**	F	48 h	63	2:1
4	$Ph_2N(CO)Cl$	**4j**	F	48 h	87	1:1
4	$ClSO_2NCO$	**4k**	A	1 min	100	1:3
5	Cl_3AcNCO	**5a**	A	1 min	100	1:4
5a		**5b**	B	1 h	95	1:4
5	ClAcNCO	**5c**	A	1 min	100	1:4
5	EtNCO	**5e**	D	40 min	93	1:4
5	AllNCO	**5f**	D	20 min	80	1:4
5	PhNCO	**5g**	D	40 min	88	1:4
1	$ClSO_2NCO$	**5k**	A	1 min	100	1:4
6	Cl_3AcNCO	**6a**	A	1 min	100	Only α
6a		**6b**	B	1 h	100	Only α
6	ClAcNCO	**6c**	A	1 min	100	Only α
6	EtNCO	**6e**	D	30 min	91	Only α
6	AllNCO	**6f**	D	20 min	89	Only α
6	PhNCO	**6g**	D	30 min	95	Only α
6	Im_2CO	**6h**	E	4 h	91	Only α

[a] Stereo information was remained during the reaction.

on ice and extracted with ethyl acetate. The organic layer was washed with diluted hydrochloric acid, dried over magnesium sulfate, filtered and concentrated. The residue could be purified by column chromatography eluting with a cyclohexane ethyl acetate mixture (exact ratio of the solvents depended mostly on the protecting groups of the carbohydrate, usually a 1:1 mixture was adequate).

4.8. Glycosidation of glycosyl carbamates to cyclohexyl-2,3,4,6-tetra-*O*-benzyl-α/β-D-glucopyranosid 8αβ with Lewis acids

A solution of 1.0 mmol glycosyl carbamate and 1.1 mmol of cyclohexanol was stirred in 10 mL dichloromethane with 200 mg of powdered molecular sieves 4 Å for 4 h at room temperature under an Argon atmosphere. After this period 1.0 mmol of the particular promoter ($SnCl_4$, $AlCl_3$, $FeCl_3$, $BF_3{\cdot}OEt_2$, $TrtClO_4$, MeOTf, TMSOTf or $ZnCl_2$) was added to the solution (dropwise or in small portions) under exclusion of moisture. When the reaction was finished (TLC-monitoring) sodium hydrogencarbonate was added and the reaction mixture was stirred for further 15 min. The reaction mixture was diluted with 10 mL of dichloromethane and washed with saturated sodium hydrogencarbonate solution and water. The organic layer was dried over magnesium sulfate, filtered and evaporated. The residue could be purified by column chromatography.

Table 5. Characteristics of 1-*O*-glycosyl carbamates

	Conf.	^{1}H NMR		^{13}C NMR		CHN analysis	$[\alpha]_D^{20}$ (*c* 1, $CHCl_3$) (°)	Mp (°C)
		H-1 (ppm)	–N*H*– (ppm)	C-1 (ppm)	–O*C*ONH (ppm)			
1a	α	6.30	8.50	93.92	148.51	Calcd for $C_{37}H_{36}Cl_3NO_8$ C, 60.97; H, 4.98; N, 1.92.	Mixture	Syrup
	β	5.57	8.35	95.78	148.47	Found: α and β: C, 60.92; H, 4.94; N, 1.96		
1b	α	6.15	4.78	91.03	154.89	Calcd for $C_{35}H_{37}NO_7$ C, 72.02; H, 6.39; N, 2.40.	Mixture	84–87
	β	5.46	4.75–5.09	95.24	154.45	Found: α and β C, 71.98; H, 6.27; N, 2.30		
1c	α	6.24	8.00	93.14	149.69	Calcd for $C_{37}H_{38}ClNO_8$ C, 70.30; H, 6.06; N, 2.22.	+17.1	118–119
	β	5.51	7.56	95.80	149.59	Found: α: C, 70.35; H, 5.97; N, 2.14 β: C, 70.21; H, 5.99; N, 2.08	−12.2	118–119
1d	α	6.20	7.44	92.50	150.36	Calcd for $C_{37}H_{39}NO_8$ C, 74.35; H, 6.58; N, 2.34.	+15.7	Syrup
	β	5.52	7.20	95.18	150.24	Found: α: C, 74.19; H, 6.52; N, 2.26 β: C, 74.21; H, 6.50; N, 2.28	+21.9	Syrup
1e	α	6.20	4.86	90.45	154.34	Calcd for $C_{37}H_{41}NO_7$ C, 72.65; H, 6.76; N, 2.29.	+15.1	Syrup
	β	5.49	4.58	95.03	154.07	Found: α: C, 72.80; H, 6.83; N, 2.29 β: C, 72.54; H, 6.60; N, 2.15	+37.8	Syrup
1f	α	6.21	4.84	90.82	154.40	Calcd for $C_{38}H_{41}NO_7$ C, 73.17; H, 6.63; N, 2.25.	+55.1	109–115
	β	5.50	4.67	95.23	154.10	Found: α: C, 73.11; H, 6.60; N, 2.19 β: C, 73.09; H, 6.55; N, 2.15	+0.8	98
1g	α	6.27	6.68	91.15	151.51	Calcd for $C_{41}H_{41}NO_7$ C, 74.46; H, 6.26; N, 2.12.	+12.2	87–90
	β	5.55	6.42	95.06	151.24	Found: α: C, 74.52; H, 6.20; N, 2.07 β: C, 74.30; H, 6.22; N, 2.05	+15.7	87–90
1h	α	6.44	—	94.86	—	Calcd for $C_{41}H_{41}NO_7$ C, 71.91; H, 6.03; N, 4.41.	Mixture	Syrup
	β	5.76		96.93		Found: α and β C, 71.82; H, 5.91; N, 4.39		
1i	α	6.40	—	90.88	154.08	Calcd for $C_{39}H_{45}NO_7$ C, 73.22; H, 7.09; N, 2.19.	+4.2	Syrup
	β	5.64		95.41	153.43	Found: α and β C, 73.58; H, 7.21; N, 2.58	+6.1	Syrup
1j	α	6.41	—	92.16	152.99	Calcd for $C_{47}H_{45}NO_7$ C, 76.71; H, 6.16; N, 1.90.	+100.6	Syrup
	β	5.65		99.11	155.72	Found: α and β C, 75.28; H, 6.87; N, 2.36	+42.3	Syrup
2a	α	7.10	8.49	95.26	158.84	Calcd for $C_{49}H_{44}Cl_3NO_8$ C, 66.78; H, 5.03; N, 1.59.	Mixture	Syrup
	β	6.32	8.65	97.68	157.93	Found: α and β C, 66.21; H, 4.87; N, 1.65		
2b	α	6.39	6.24–6.52	90.24	154.61	Calcd for $C_{28}H_{31}NO_7$ (6-acetate) C, 68.14; H, 6.33; N, 2.84.	Mixture	Syrup
	β	5.59	6.24–6.52	96.67	154.50	Found: α and β C, 69.12; H, 5.98; N, 2.76		
2c	α	6.44	8.00	96.59	150.13	Calcd for $C_{49}H_{46}ClNO_8$ C, 72.45; H, 5.71; N, 1.72.	+67.4	71
	β	5.50	7.52	93.79	150.13	Found: α and β C, 75.48; H, 6.39; N, 1.78	Not pure	Syrup
2e	α	6.18	4.73	86.27	154.03	Calcd for $C_{49}H_{46}NO_7$ C, 77.04; H, 6.47; N, 1.83.	Mixture	78
	β	5.61	4.70	92.37	154.03	Found: α and β C, 77.54; H, 6.39; N, 1.78		
2f	α	6.27	4.84	92.53	154.00	Calcd for $C_{50}H_{49}NO_7$ C, 77.40; H, 6.37; N, 1.81.	Mixture	63
	β	5.65	4.67	95.23	154.10	Found: α and β C, 77.84; H, 6.39; N, 1.78		

(*continued on next page*)

Table 5 (*continued*)

	Conf.	^{1}H NMR		^{13}C NMR		CHN analysis	$[\alpha]_D^{20}$ (*c* 1, $CHCl_3$) (°)	Mp (°C)
		H-1 (ppm)	–N*H*– (ppm)	C-1 (ppm)	–O*C*ONH (ppm)			
2g	α	6.42	6.58	91.71	152.02	Calcd for $C_{53}H_{49}NO_7$ C, 78.40; H, 6.08; N, 1.73.	+86.8	76
	β	5.59	6.44	95.81	151.72	Found: α and β C, 78.84; H, 6.39; N, 1.78	−11.2	100
3a	α	6.27	8.17	95.57	148.10	Calcd for $C_{46}H_{48}Cl_3NO_8Si$ C, 62.97; H, 5.51; N, 1.60. Found: C, 62.83; H, 5.45; N, 1.63	+17.8	Syrup
3b	α	6.14	4.77–4.83	92.84	154.74	Calcd for $C_{44}H_{50}NO_7Si$ C, 72.10; H, 6.88; N, 1.91. Found: C, 72.01; H, 7.95; N, 1.88	+5.1	Syrup
3c	α	6.18	8.25	94.62	149.35	Calcd for $C_{46}H_{50}ClNO_8Si$ C, 68.34; H, 6.23; N, 1.73.	+40.3	Syrup
	β	5.57	7.44	94.29	149.33	Found: α: C, 68.41; H, 6.22; N, 1.69 β: C, 68.30; H, 6.20; N, 1.59	−5.5	
4a	α	6.42	8.79	91.45	147.41	Calcd for $C_{17}H_{20}Cl_3NO_{12}$ C, 60.97; H, 4.98; N, 1.92.	Mixture	Syrup
	β	5.81	8.85	93.34	147.46	Found: C, 60.92; H, 4.94; N, 1.96		
4b	α	6.21	5.06–5.20	90.04	154.27	Calcd for $C_{15}H_{21}NO_{11}$ C, 46.04; H, 5.41; N, 3.58.	Mixture	Syrup
	β	5.65		92.91	154.17	Found: α and β C, 45.87; H, 5.32; N, 3.50		
4c	α	6.33	8.54	91.66	149.32	Calcd for $C_{17}H_{22}ClNO_{12}$ C, 46.43; H, 5.04; N, 3.18.	−8.6	Syrup
	β	5.71	8.91	93.34	149.38	Found: α: C, 46.26; H, 5.09; N, 3.07 β: C, 46.26; H, 5.09; N, 3.06	+67.8	Syrup
4e	α	6.33	5.06–5.34	90.44	153.50	Calcd for $C_{17}H_{25}NO_{11}$ C, 48.69; H, 6.01; N, 3.34.	+5.3	Syrup
	β	5.68	5.07	92.60	153.43	Found β: C, 48.71; H, 6.10; N, 3.30	+13.3	Syrup
4f	α	6.24	5.06–5.18	89.77	153.62	Calcd for $C_{18}H_{25}NO_{11}$ C, 50.12; H, 5.84; N, 3.25.	+44.3	Syrup
	β	5.69	5.06–5.18	92.70	153.53	Found β: C, 50.07; H, 5.79; N, 3.22	+8.9	Syrup
4g	α	6.35	7.19	89.97	150.66	Calcd for $C_{21}H_{25}NO_{11}$ C, 53.96; H, 5.39; N, 3.00.	+45.1	Syrup
	β	5.70	7.19	92.97	150.53	Found α: C, 53.81; H, 5.30; N, 2.93	+61.9	Syrup
4h	α	6.51	—	94.86	—	Calcd for $C_{18}H_{22}N_2O_{11}$ C, 48.87; H, 5.01; N, 6.33.	Mixture	Syrup
	β	5.85		96.93		Found: α and β C, 48.73; H, 4.92; N, 6.24		
4i	α	6.28	—	90.04	153.09	Calcd for $C_{19}H_{29}NO_{11}$ C, 51.00; H, 6.53; N, 3.13.	Mixture	Syrup
	β	5.68		92.95	153.14	Found: α and β C, 49.32; H, 6.22; N, 3.36		
4j	α	6.33	—	93.41	152.15	Calcd for $C_{27}H_{29}NO_{11}$ C, 59.66; H, 5.38; N, 2.58.	Mixture	Syrup
	β	5.75		90.82	151.81	Found: α and β C, 60.23; H, 5.63; N, 3.26		
5a	α	6.47	8.66	90.65	147.42	Calcd for $C_{17}H_{20}Cl_3NO_{12}$ C, 38.04; H, 3.76; N, 2.61.	Mixture	Syrup
	β	5.77	8.78	94.25	147.43	Found: C, 37.89; H, 3.71; N, 2.70		Syrup
5b	α	6.27	4.87–5.10	93.44	153.93	Calcd for $C_{15}H_{21}NO_{11}$ C, 46.04; H, 5.41; N, 3.58.	Mixture	Syrup
	β	5.63	4.91	93.44	153.93	Found: α and β C, 45.90; H, 5.36; N, 3.49		
5c	α	6.37	8.57	92.37	149.47	Calcd for $C_{17}H_{22}ClNO_{12}$ C, 46.43; H, 5.04; N, 3.18.	+53.3	Syrup
	β	5.67	8.62	94.02	149.15	Found: α: C, 46.30; H, 4.98; N, 3.11 β: C, 46.29; H, 4.90; N, 3.20	+20.0	Syrup
5e	α	6.28	4.89–5.18	90.14	153.93	Calcd for $C_{17}H_{25}NO_{11}$ C, 48.69; H, 6.01; N, 3.34.	+23.6	Syrup
	β	5.63	5.18	92.97	153.46	Found β: C, 48.67; H, 5.98; N, 3.30	+ 63.4	Syrup

Table 5 (*continued*)

	Conf.	^{1}H NMR		^{13}C NMR		CHN analysis	$[\alpha]_D^{20}$ (*c* 1, $CHCl_3$) (°)	Mp (°C)
		H-1 (ppm)	–N*H*– (ppm)	C-1 (ppm)	–O*C*ONH (ppm)			
5f	α	6.23	4.98	90.53	153.78	Calcd for $C_{18}H_{25}NO_{11}$ C, 50.12; H, 5.84; N, 3.25.	+81.6	Syrup
	β	5.60	5.14	93.19	153.16	Found: α: C, 50.17; H, 5.82; N, 3.25β: C, 50.00; H, 5.76; N, 3.04	+19.1	131
5g	α	6.40	7.04–7.47	90.61	150.76	Calcd for $C_{21}H_{25}NO_{11}$ C, 53.96; H, 5.39; N, 3.00.	+8.9	Syrup
	β	5.76	7.04–7.47	93.11	150.76	Found β: C, 53.85; H, 5.33; N, 3.03	+21.3	Syrup
6a	α	6.13	8.55	103.37	148.29	Calcd for $C_{15}H_{20}Cl_3NO_8$ C, 40.34; H, 4.51; N, 3.14. Found: C, 40.21; H, 4.48; N, 3.10	+12.6	Syrup
6b	α	6.09	4.86	101.36	154.13	Calcd for $C_{13}H_{21}NO_7$ C, 51.82; H, 7.02; N, 4.65. Found: C, 51.61; H, 7.02; N, 4.60	−8.7	127
6c	α	6.14	8.02	103.05	149.52	Calcd for $C_{15}H_{22}ClNO_8$ C, 51.51; H, 6.34; N, 4.00. Found: C, 51.43; H, 6.28; N, 3.89	+30.5	Syrup
6e	α	6.08	4.74	101.13	151.10	Calcd for $C_{15}H_{25}NO_7$ C, 54.70; H, 7.65; N, 4.25. Found: C, 54.51; H, 7.61; N, 4.22	+29.9	Syrup
6f	α	6.09	4.86	101.36	154.13	Calcd for $C_{16}H_{25}NO_7$ C, 56.30; H, 7.38; N, 4.10. Found: C, 56.20; H, 7.31; N, 4.09	+77.1	Syrup
6g	α	6.08	7.11	101.46	151.37	Calcd for $C_{19}H_{25}NO_6$ C, 60.47; H, 6.68; N, 3.71. Found: C, 60.38; H, 6.63; N, 3.62	+45.7	Syrup
6h	α	6.33	—	—	—	Calcd for $C_{16}H_{22}N_2O_7$ C, 54.54; H, 6.24; N, 7.95. Found: C, 54.40; H, 6.19; N, 7.83	+22.0	Syrup

All compounds display the expected spectroscopic data including ^{1}H NMR, ^{13}C NMR and optical rotation. In this table only the characteristic signals are presented.

4.8.1. Cyclohexyl-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (8α). Colourless syrup; $R_f = 0.38$ (cyclohexane/ethyl acetate = 3:1). ^{1}H NMR ($CDCl_3$): δ 1.07–1.90 (m, 10H, cyclohexyl-H), 3.42–3.54 (m, 1H, cyclohexyl-H-1), 3.49 (dd, 1H, $^3J_{H4,H3}$ 9.2, $^3J_{H4,H5}$ 10.4,H-4), 3.49 (dd, 1H, $^3J_{H6,H5}$ 4.0, $^2J_{H6,\ H6'}$ 9.2, H-6), 3.56 (dd, 1H, $^3J_{H6',H5}$ 2.2, $^2J_{H6',H6}$ 9.2, H-6′), 3.66 (dd, 1H, $^3J_{H2,H1}$ 4.0, $^3J_{H2,H3}$ 10.4, H-2), 3.81 (ddd, 1H, $^3J_{H5,H6'}$ 2.2, $^3J_{H5,H6}$ 4.0, $^3J_{H5,H4}$ 10.4, H-5), 3.93 (dd, 1H, $^3J_{H3,H4}$ 9.2, $^3J_{H3,H2}$ 10.4, H-3), 4.39 (d, 1H, $^2J_{PhCH_2}$ 12.4, $PhCH_2$), 4.58 (d, 1H, $^2J_{PhCH_2}$ 12.4, $PhCH_2$), 4.66 (d, 1H, $^2J_{PhCH_2}$ 12.4, $PhCH_2$), 4.73 (d, $^3J_{H1,H2}$ 4.0, 1H, H-1), 4.92 (d, 1H, $^2J_{PhCH_2}$ 11.2, $PhCH_2$), 7.04–7.35 (m, 20H, Ar–H).

4.8.2. Cyclohexyl-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (8β). Colourless syrup; $R_f = 0.38$ (cyclohexane/ethyl acetate = 3:1). ^{1}H NMR ($CDCl_3$): δ 1.09–2.08 (m, 10H, cyclohexyl-H), 3.39–3.77 (m, 7H, H-2, H-3, H-4, H-5, H-6, H-6′, cyclohexyl-H-1), 4.49 (d, 1H, $^3J_{H1,H2}$ 8.0, H-1), 4.52 (d, 1H, $^2J_{PhCH_2}$ 10.8, $PhCH_2$), 4.54 (d, 1H, $^2J_{PhCH_2}$ 12.4, $PhCH_2$), 4.60 (d, 1H, $^2J_{PhCH_2}$ 12.4, $PhCH_2$), 4.70 (d, 1H, $^2J_{PhCH_2}$ 10.8, $PhCH_2$), 4.76 (d, 1H, $^2J_{PhCH_2}$ 11.2, $PhCH_2$), 4.80 (d, 1H, $^2J_{PhCH_2}$ 11.2, $PhCH_2$), 4.91 (d, 1H, $^2J_{PhCH_2}$ 11.4 $PhCH_2$), 4.98 (d, 1H, $^2J_{PhCH_2}$ 11.4, $PhCH_2$), 7.12–7.39 (m, 20 H, Ar–H). Calcd for $C_{40}H_{46}O_6$: C, 77.14; H, 7.44. Found: C, 77.50; H, 7.45.

4.9. Glycosidation of glycosyl carbamates to cyclohexyl-2,3,4,6-tetra-*O*-benzyl-α/β-D-glucopyranosid (8αβ) with $Cu(OTf)_2$ and $Sn(OTf)_2$

In contrast to the method mentioned above the reaction was carried out in diethylether. The ratio of the promoter was increased after 4 h up to 5 equiv without detectable reaction.

4.10. (a) Glycosidation of glycosyl carbamates (general procedure)

A solution of 1.0 mmol glycosyl carbamate and 1.1 mmol of the glycosyl acceptor was stirred in 10 mL dichloromethane with 200 mg of powdered molecular sieves 4 Å for 4 h at room temperature under an Argon atmosphere. After this period 1.0 mmol of $SnCl_4$ was added to the solution dropwise under exclusion of moisture. When the reaction was finished (TLC-monitoring)

sodium hydrogencarbonate was added and the reaction mixture was stirred for further 15 min. The reaction mixture was diluted with 10 mL dichloromethane and washed with saturated sodium hydrogencarbonate solution and water. The organic layer was dried over magnesium sulfate, filtered and evaporated. The residue could be purified by column chromatography.

(b) One-pot procedure for glycosidation starting from *N*-trichloroacetyl- and *N*-chloroacetyl 1-*O*-glycosyl carbamates. The acyl isocyanate (1.1 mmol) was added to a solution of the corresponding carbohydrate derivative (1 mmol) in 10 mL of dry dichloromethane at room temperature under an argon atmosphere. The reaction was complete after 1 min reaction time (TLC-monitoring). To this solution 1.1 mmol of the glycosyl acceptor and 200 mg of powdered molecular sieves 4 Å were added. The reaction mixture was stirred for 4 h at room temperature. After this period 1.0 mmol of $SnCl_4$ was added to the solution dropwise under exclusion of moisture. When the reaction was finished (TLC-monitoring) sodium hydrogencarbonate was added and the reaction mixture was stirred for further 15 min. The reaction mixture was diluted with 10 mL dichloromethane and washed with saturated sodium hydrogencarbonate solution and water. The organic layer was dried over magnesium sulfate, filtered and evaporated. The crude disaccharide could be purified by column chromatography.

4.10.1. Methyl 6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (10α). Colourless syrup; $R_f = 0.15$ (cyclohexane/ethyl acetate = 6:1). ^{1}H NMR ($CDCl_3$): δ 3.35 (s, 3 H, OCH_3), 3.44 (dd, 1H, $^3J_{H1,H2}$ 3.5 Hz, $^3J_{H2,H3}$ 9.5 Hz, H-2a), 3.53 (dd, 1H, $^3J_{H1,H2}$ 3.7 Hz, $^3J_{H2,H3}$ 9.2 Hz, H-2b), 3.56–3.60 (m, 1H, H-4b), 3.60–3.70 (m, 3 H, H-4a, H-5a, H-6a), 3.71–3.86 (m, 4 H, H-5b, H-6b, H-6′b, H-6′a), 3.94–3.98 (m, 1H, H-3a), 3.97–4.01 (m, 1H, H-3b), 4.39–4.98 (m, 14H, $PhCH_2$), 4.56 (d, 1H, $^3J_{H1,H2}$ 3.5 Hz, H-1a), 4.97 (d, 1H, $^3J_{H1,H2}$ 3.7 Hz, H-1b), 7.10–7.40 (m, 35 H, Ar–H).

4.10.2. Methyl 6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-β-D-glucopyranoside (10β). Colourless syrup; $R_f = 0.15$ (cyclohexane/ethyl acetate = 6:1). Only clear ^{1}H NMR peaks are listed. ^{1}H NMR ($CDCl_3$): δ 3.32 (s, 3H, OCH_3), 3.40–3.71 (m, 6H, H-4a, H-5a, H-6a, H – $6'_a$, H-3b, H-6b), 3.45–3.51 (m, 1H, H-2b), 3.52 (dd, 1H, $^3J_{H1,H2}$ 3.6 Hz, $^3J_{H2,H3}$ 9.5 Hz, H-2b), 3.57–3.61 (m, 1H, H-4b), 3.82 (ddd, 1H, $^3J_{H5,H6'}$ 0.9 Hz, $^3J_{H5,H6}$ 4.5 Hz, $^3J_{H4,H5}$ 9.9 Hz, H-5b), 3.99 (dd, 1H, $^3J_{H3,H4}$ 9.0 Hz, $^3J_{H2,H3}$ 9.5 Hz, H-3a), 4.18 (dd, 1H, $^3J_{H5,H6'}$ 1.4 Hz, $^3J_{H6,H6'}$ 11.2 Hz, H-6′b), 4.34 (d, 1H, $^3J_{H1,H2}$ 7.8 Hz, H1-b), 4.48–5.00 (m, 14 H, $PhCH_2$), 4.60 (d, 1H, $^3J_{H1,H2}$ 3.6 Hz, H-1a), 7.13–7.37 (m, 35 H, Ar–H).

4.10.3. Methyl 6-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (11β). Colourless syrup; $R_f = 0.24$ (cyclohexane/ethyl acetate = 3:2). $[\alpha]_D^{20}$ −3.0 (*c* 1.4, $CHCl_3$). Only clear ^{1}H NMR peaks are listed. ^{1}H NMR ($CDCl_3$): δ 1.95, 1.99, 2.01, 2.01 (4s, 12H, $4CH_3CO$), 3.36 (s, 3H, OCH_3), 3.51 (dd, 1H, $^3J_{H1,H2}$ 3.7 Hz, $^3J_{H2,H3}$ 9.8 Hz, H-2a), 4.52 (d, 1H, $^3J_{H1,H2}$ 7.9 Hz, H-1b), 4.58 (d, 1H, $^3J_{H1,H2}$ 3.7 Hz, H-1a), 5.08 (dd ('t'), 1H, ^3J 9.5 Hz, H-4), 5.17 (dd ('t'), 1H, ^3J 9.5 Hz, H-3), 5.31 (dd, 1H, $^3J_{H1,H2}$ 7.9 Hz, $^3J_{H2,H3}$ 9.5 Hz, H-2).

4.10.4. Methyl 6-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,4-tri-*O*-benzyl-β-D-glucopyranoside (12β). Colourless syrup; $R_f = 0.30$ (cyclohexane/ethyl acetate = 1:1). $[\alpha]_D^{20}$ +7.0 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ Gluc.: 3.36 (dd, 1H, *J* 9.0 Hz, *J* 9.4 Hz, H-4), 3.40 (dd, 1H, *J* 3.7 Hz, *J* 9.0 Hz, H-2), 3.51 (ddd, 1H, *J* 1.8 Hz, *J* 4.0 Hz, *J* 9.4 Hz, H-5), 3.58 (s, 3H, OCH_3), 3.64 (dd, 1H, *J* 9.0 Hz, *J* 9.0 Hz, H-3), 4.12 (dd, 1H, *J* 4.0 Hz, *J* 12.1 Hz, H-6), 4.12 (dd, 1H, *J* 1.8 Hz, *J* 12.1 Hz, H-6′), 4.61 (d, 1H, *J* 3.7 Hz, H-1); Gal.: δ 1.92, 1.97, 1.99, 2.07 (4s, 12H, $4CH_3CO$), 3.66 (dd, 1H, *J* 7.0 Hz, *J* 11.0 Hz, H-6′), 3.87 (ddd, 1H, *J* 0.9 Hz, *J* 7.0 Hz, *J* 7.0 Hz, H-5), 4.12 (dd, 1H, *J* 7.0 Hz, *J* 11.0 Hz, H-6), 4.29 (d, 1H, *J* 7.0 Hz, H-1), 4.98 (dd, 1H, *J* 3.4 Hz, *J* 10.4 Hz, H-3), 5.36 (dd, 1H, *J* 3.7 Hz, *J* 10.4 Hz, H-2), 5.38 (dd, 1H, *J* 0.9 Hz, *J* 3.4 Hz, H-4).

4.10.5. Methyl 4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (14α). Colourless syrup; $R_f = 0.15$ (cyclohexane/ethyl acetate = 6:1). Only clear ^{1}H NMR peaks are listed. ^{1}H NMR ($CDCl_3$): δ 3.37 (s, 3H, OCH_3), 3.43 (dd, 1H, $^3J_{H1,H2}$ 3.0 Hz, $^3J_{H2,H3}$ 9.5 Hz, H-2a), 3.48 (dd, 1H $^3J_{H1,H2}$ 3.6 Hz, $^3J_{H2,H3}$ 9.4 Hz, H-2b), 4.02 (dd, 1H, $^3J_{H3,H4}$ 9.2 Hz, $^3J_{H2,H3}$ 9.5 Hz, H-3a), 4.27–5.05 (m, 14H, 7 × OCH_2Ph), 5.69 (d, 1H, $^3J_{H1,H2}$ 3.6 Hz, H-1b), 7.05–7.30 (m, 35H, Ar–H).

4.10.6. Methyl 4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (14β). Colourless syrup; $R_f = 0.15$ (cyclohexane/ethyl acetate = 6:1). Only clear ^{1}H NMR peaks are listed. ^{1}H NMR ($CDCl_3$): δ 3.36 (s, 3H, OCH_3), 3.71 (dd, 1H, $^3J_{H5,H6}$ 1.5 Hz, $^3J_{H6,H6'}$ 11.0 Hz, H-6a), 4.40 (d, 1H, $^3J_{H1,H2}$ 7.0 Hz, H-1b), 4.35–4.62 (m, 6 H, 3 × OCH_2Ph), 4.55 (d, 1H, $^3J_{H1,H2}$ 3.0 Hz, H-1a), 4.71–4.82 (m, 6H, 3 × OCH_2Ph), 4.87 (d, $^2J_{PhCH_2}$ 11.2 Hz, 1H, OCH_2Ph), 5.09 (d, 1H, $^2J_{PhCH_2}$ 11.2 Hz, OCH_2Ph), 7.17–7.45 (m, 35H, Ar–H). Calcd for $C_{62}H_{66}O_{11}$: C, 75.43; H, 6.74. Found: C, 75.88; H, 6.83.

4.10.7. Methyl 4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (15β). Colourless syrup; $R_f = 0.22$ (cyclohexane/ethyl ace-

tate = 1:3). $[\alpha]_D^{20}$ −5.0 (*c* 1.0, $CHCl_3$). Only clear ^1H NMR peaks are listed. ^1H NMR ($CDCl_3$): δ 1.94, 1.99, 2.01, 2.03 (4s, 12H, $4CH_3CO$), 3.42 (dd, 1H, *J* 3.7 Hz, *J* 9.1 Hz, H-2′), 3.60 (dd, 1H, *J* 8.6 Hz, *J* 9.1 Hz, H-3′), 3.69 (s, 3H, CH_3CO), 3.98 (dd, 1H, *J* 8.6 Hz, *J* 9.9 Hz, H-4′), 4.31 (d, 1H, *J* 7.8 Hz, H-1), 4.70 (d, 1H, *J* 3.7 Hz, H-l′), 4.95 (dd, 1H, *J* 7.8 Hz, *J* 9.4 Hz, H-2).

4.10.8. Methyl 4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (16β). Colourless syrup; R_f = 0.29 (cyclohexane/ethyl acetate = 1:3). $[\alpha]_D^{20}$ +8.0 (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$): Gluc.: δ 3.40 (dd, 1H, *J* 3.7 Hz, *J* 9.0 Hz, H-2), 3.56 (s, 3H, OCH_3), 3.57 (dd ('t'), 1H, *J* 9.0 Hz, *J* 9.5 Hz, H-4), 3.96 (dd, 1H, *J* 9.0 Hz, *J* 9.5 Hz, H-3), 4.28 (d, 1H, *J* 3. 7 Hz, H-1); Gal: δ = 1.91, 1.97, 1.99, 2.07 (4s, 12H, $4CH_3CO$), 3.53 (ddd, 1H, *J* 1.3 Hz, *J* 8.1 Hz, *J* 8.5 Hz, H-5), 3.84 (dd, 1H, *J* 8.5 Hz, *J* 12.4 Hz, H-6′), 4.64 (d, 1H, *J* 8.0 Hz, H-1), 4.84 (dd, 1H, *J* 3.6 Hz, *J* 10.5 Hz, H-3), 5.12 (dd, 1H, *J* 8.0 Hz, *J* 10.5 Hz, H-2), 5.26 (dd, 1H, *J* 1.3 Hz, *J* 3.6 Hz, H-4).

Acknowledgements

We are grateful to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for providing financial support. We are also very grateful to Mrs. Beate Gröne for her support during this project.

References

1. Greene, T. W.; Wuts, P. G. M. *Protecting Groups in Organic Synthesis*; Wiley: New York, 1991.
2. Kunz, H.; Zimmer, J. *Tetrahedron Lett.* **1993**, *34*, 2907–2910.
3. Hinklin, R. J.; Kiessling, L. L. *J. Am. Chem. Soc.* **2001**, *123*(4), 3379–3380.
4. (a) Plusquellec, D.; Roulleau, F.; Brown, E. *Tetrahedron Lett.* **1984**, *25*, 1901–1904; (b) Plusquellec, D.; Lefeuvre, M. *Tetrahedron Lett.* **1987**, *28*, 4165–4168; (c) Lenders, R. G. G.; Ruytenbeek, R.; Damen, E. W. P.; Scheeren, H. W. *Synthesis* **1996**, 1309–1312; (d) Prata, C.; Mora, N.; Lacombe, J.-M.; Maurizis, J. C.; Pucci, B. *Tetrahedron Lett.* **1997**, *38*(51), 8859–8862; (e) Prata, C.; Mora, N.; Lacombe, J.-M.; Maurizis, J. C.; Pucci, B. *Carbohydr. Res.* **1999**, *321*, 4–14.
5. (a) Perrine, T. D.; Claudemans, C. P. J.; Ness, R. K.; Kyle, J., Jr.; Fletcher, H. G., Jr. *J. Org. Chem.* **1967**, *32*, 664–669; (b) Eby, R.; Sondheimer, S. J.; Schuerch, C. *Carbohydr. Res.* **1979**, *73*, 273–276; (c) Sakai, J.-I.; Takeda, T.; Ogihara, Y. *Carbohydr. Res.* **1981**, *95*, 125–131; (d) Chaudhary, S. K.; Hernandez, O. *Tetrahedron Lett.* **1979**, *1*, 95–98; (e) Bessodes, M.; Komiotis, D.; Antonakis, K. *Tetrahedron Lett.* **1986**, *27*, 579–580; (f) *Organikum,* 15th ed.; Deutscher Verlag der Wissenschaften: Berlin, 1984; pp 511–512; (g) Schmidt, O. T. *Methods Carbohydr. Chem.* **1963**, *2*, 318–325.
6. Schmidt, R. R.; Michel, J. *Angew. Chem.* **1980**, *92*, 763–764; Schmidt, R. R.; Michel, J. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 731.
7. When an excess of ethyl isocyanates is used with carbohydrate derivatives **4**, **5** and **6** or allyl isocyanate with **6** the formation of the corresponding allophanates is obtained within 60 min in 90% yield under typical reaction conditions (method D).
8. (a) Staab, H. A. *Liebigs Ann. Chem.* **1957**, *609*, 83–88; (b) Staab, H. A. *Angew. Chem.* **1962**, *12*, 407–423; Staab, H. A. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 351–367.
9. Schmidt, R. R. *Adv. Carbohydr. Chem.* **1994**, *50*, 21.
10. Ford, M. J.; Ley, S. V. *Synlett* **1990**, 255–256.
11. Pearson, R. G. *J. Am. Chem. Soc.* **1963**, *85*, 3533–3539; Pearson, R. G. *Coord. Chem. Rev.* **1990**, *100*, 403–425.
12. Hanessian, S.; Baquet, C.; Lehong, N. *Carbohydr. Res.* **1980**, *80*, C17–C22.
13. Fraser-Reid, B.; Konradsson, P.; Mootoo, D. R.; Udodong, U. E. *J. Chem. Soc., Chem. Commun.* **1988**, 823–825.
14. Mallet, J.-M.; Meyer, G.; Yvelin, F.; Jutand, A.; Amatore, C.; Sinaÿ, P. *Carbohydr. Res.* **1993**, *244*, 237–246.
15. Küster, J. M.; Dyong, I. *Liebigs Ann. Chem.* **1975**, 2179–2189.
16. Isbell, H. S. *Annu. Rev. Biochem.* **1940**, *9*, 65–92.
17. See, for example: Lemieux, R. U. *Adv. Carbohydr. Chem.* **1954**, *9*, 1–57.
18. Dichloromethane was distilled over CaH_2.