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PII: S0032-3861(97)00443-6

Polymer Vol. 39 Nos. 8–9, pp. 1617–1629, 1998

0032-3861/97/$17.00+0.00

Synthesis of aldonamide siloxanes by hydrosilylation

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(Received 14 March 1997; revised 22 May 1997)

The synthesis of hydrophobic/hydrophilic hybrid polymers based on polydimethylsiloxanes (PDMS) and carbohydrate derivatives involving a hydrosilylation step is reported. Starting with poly(dimethyl-*co*-hydromethyl)siloxanes (PDMS-*co*-HMS), *O*-acetylated *N*-allylaldonamides of various sugars can be attached to the siloxane backbone using platinum catalysts. The characteristics of different transition metal complexes in the polymer-analogous formation of Si–C bonds are investigated. A generalized reaction pathway applicable to several reducing carbohydrates is established to synthesize aldonamide siloxanes in a broad variety of molecular weight and composition. The products obtained, "sweet siloxanes", are characterized by g.p.c., *FT*i.r. spectrometry and ^{13}C n.m.r. spectroscopy. © 1997 Elsevier Science Ltd. All rights reserved.

(Keywords: Aldonamide siloxanes; hydrosilylation; transition metal complexes)

INTRODUCTION

Hybrid materials composed of a synthetic polymer backbone and covalently linked carbohydrate moieties have attracted increasing interest in recent years. Polystyrene containing lactobionamide side chains can be used as a cell culture medium, allowing hepatocytes to survive for several days[1]. Polydimethylsiloxanes (PDMS) crosslinked by sucrose units exhibit excellent biocompatibility and also good mechanical and optical properties. These materials are suitable for the manufacture of contact lenses. These modified siloxanes have also been used successfully as cell culture media[2]. In previous work we described the synthesis of modified siloxanes in which the carbohydrates are coupled as *O*-glycosides[3]. In this paper we report the possibilities of the synthesis of polydimethylsiloxanes statistically modified with carbohydrate derivatives more specifically with aldonic acid amides, which incorporate the amide as a part of the covalent linking group (*Scheme 1*).

This strategy provides a chemical structure which is inert towards hydrolysis and oxidation under normal conditions. Furthermore, the linking at C-1 of an aldonic acid minimizes difficulties regarding regio- and stereoselectivity, especially when oligosaccharides are applied. If 1-*O*-glycosides are used, one often encounters the problem of separating α- and β-anomers, a task which is not easy to fulfil. According to our experience, this is very difficult to achieve in the case of maltoheptaose (Glc_7, **1**) and cannot be accomplished by standard flash chromatography. Upon derivatization of the carbohydrate to the corresponding aldonic acid (*O*-unprotected lactone $\mathbf{2_n}$, *O*-acetylated lactone $\mathbf{3_n}$) it is easy to perform chemical reactions at C-1 (and O-1) while leaving the other 22 hydroxy-groups of the molecule untouched. The resulting ester or amide no longer has a chiral centre at C-1, thus the desired single product arises. This fact simplifies purification procedures, because any byproducts differ in their chemical structure and not only in stereochemistry.

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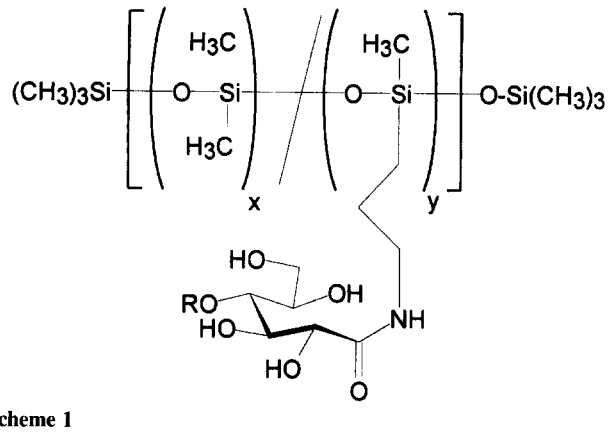
As reported previously[4,5], the modification of polydimethylsiloxanes with statistically distributed maltoheptaonamide side groups can proceed using two different strategies: either *O*-acetylated maltoheptaonolactone **3** is added to an aminopropyl functionalized PDMS (GP-4 from Genesee Polymers; see *Scheme 2*, path I) or *O*-acetylated *N*-allylmaltoheptaonamide **4** is attached via its terminal double bond in a hydrosilylation step to the Si–H groups of a poly(dimethyl-*co*-hydromethyl)siloxane backbone (see *Scheme 2*, path II). Following the first pathway, the title structure is obtained during the polymer-analogous addition reaction, i.e. formation of an amide from the primary amino groups of GP-4 and the lactone. Following the latter, the amide structure is completely built up during the procedure of derivatization of the carbohydrate with low molecular weight substrates.

RESULTS AND DISCUSSION

Synthetic pathways

Because aminopropyl functionalized PDMS are commercially available only in a small range of composition and molecular weight (Genesee Polymers' GP-4; D.P. 62; four Si–H groups per chain, as stated by the manufacturer), the direct addition of the lactone **3** does not give access to a broad variety of materials.

To obtain a wide variety of molecular weight and composition, the synthesis has to start with PDMS-*co*-HMS, which can be obtained from a cationic equilibration reaction with fairly narrow molecular weight distribution (typically $\overline{M_w}/\overline{M_n} \approx 1.4$–$1.8$ according to g.p.c. analysis, see *Table 1*). The content of Si–H groups could be varied from zero up to 100%. The molecular weight is adjustable—independent of the composition—in the range from < 7 kg mol^{-1} to > 110 kg mol^{-1}, as far as investigated. To indicate these two variables in a single abbreviation we refer to the siloxanes as *subst*-[Si$\overline{P_w}/\bar{n}$], where *subst* indicates the actual substituent (e.g. the aldonamide or—if not present—the Si–H group), $\overline{P_w}$ is the weight average of the degree of



Scheme 1

acetylated *N*-allylaldonamide in high yield. In this five step synthesis, the two acetylation reactions, the anomeric deprotection, and the oxidation procedure can be accomplished with excellent yields regardless of the particular carbohydrate used. The crucial step of this derivatization sequence is the addition of allylamine. Under the basic conditions elimination reactions may occur, which become substantial in the case of maltose and cellobiose; thus yields in the range of only 9–19% were obtained (see *Table 2*). Surprisingly, maltoheptaose reacts in the desired way with high yield.

In contrast, the reaction pathway indicated as IIb in *Scheme 2* is of general applicability. We have investigated the behaviour of various carbohydrates (glucose, galactose, maltose, cellobiose, and maltoheptaose) in this three step

Table 1 Poly(dimethyl-*co*-hydromethyl)siloxanes synthesized by cationic equilibration

Siloxane[Si $\overline{P_w}/\bar{n}$]	Si–H content/mol %	MW calculated/g mol^{-1}	$\overline{M_w}$ by g.p.c./g mol^{-1}	$\overline{M_n}$ by GPC/g mol^{-1}	$\overline{M_w}/\overline{M_n}$
[Si 95/20]	21.0	2500	6900	3800	1.8
[Si 98/5]	5.6	3400	7180	3140	2.3
[Si 190/19]	10.0	5100	14300	7160	2.0
[Si 260/12]	4.8	10300	19100	10700	1.8
[Si 540/23]	4.3	10300	40000	28700	1.4
[Si 600/30]	5.0	10300	44100	26000	1.7
[Si 880/19]	2.2	25800	65000	34200	2.2
[Si 1500/12]	0.8	51700	112000	20900	5.4

Table 2 Yields (in % theoretical) of aldonamides upon addition of allylamine to *O*-acetylated and to unprotected aldonolactones of various carbohydrates

Carbohydrate	Glucose	Galactose	Maltose	Cellobiose	Lactose	Glc_7
O-acetylated	–[a]	47	19	9	45	**83**
unprotected	78	45	**72**	**93**	–[a]	63

[a] Not investigated.

polymerization, and $\bar{n}$ is the average number of substituents per chain.

To utilize these copolymers as starting materials suitable for the synthesis of aldonamide siloxanes, the requirements of the carbohydrate moieties are: aldonamide structure, terminal C=C double bond, and protected hydroxy-groups. These features are realized in the *O*-acetylated *N*-allylaldonamides, which are again obtained by two different synthetic pathways (see *Scheme 2*, path IIa and IIb) starting from native saccharides.

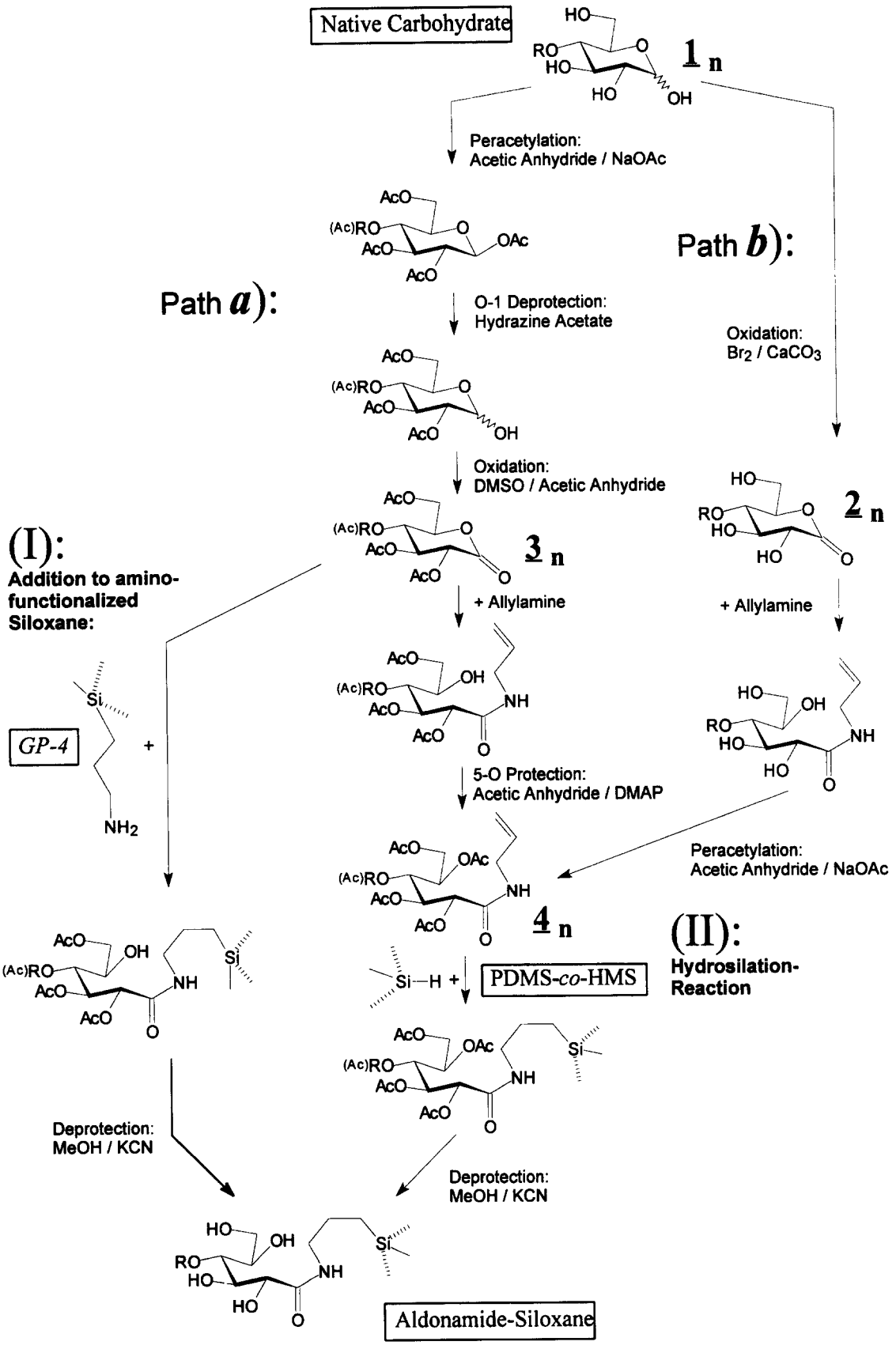
In our previous work, only two saccharides, namely glucose and maltoheptaose, were used. In this paper we report the derivatization of six different reducing carbohydrates: glucose, galactose, maltose, cellobiose, lactose, and maltoheptaose. *N*-Acetylglucosamine was also used to obtain a slightly modified carbohydrate derivative, which also incorporates an amide structure which is not part of the linking group. 3,4,6-Triacetyl-2-desoxy-2-acetamido-(β-1-*O*-allyl)-D-glucopyranose, the resulting compound **5**, was prepared from glucosamine hydrochloride or chitin via its α-acetate and α-chloride according to *Scheme 3*. **5** was also tested in the hydrosilylation reaction.

The synthesis of aldonamide derivatives according to IIa (*Scheme 2*) may also provide the acetylated lactone in the case of galactose, maltose, cellobiose, and lactose, but only with maltoheptaonolactone **3** is it possible to obtain the fully synthesis. Again the reaction with allylamine is the crucial step in the synthetic sequence, where unprotected aldonolactones are obtained as intermediates, The yields of the unprotected *N*-allylaldonamides in the case of maltose and cellobiose via IIb, as listed in *Table 2*, show a substantial increase in comparison with those from pathway IIa.

Even maltoheptaose can react this way, although purification is a little more complicated owing to the amphiphilic properties of *N*-allylmaltoheptaonamide. Whereas for mono- and disaccharides flash chromatography can be applied with good results, extremely large columns have to be used for *N*-allylmaltoheptaonamide. The performance of the separation can be improved using DEAE-Sephadex A-25/Cl^-, but in this case it is not possible to preserve the fraction containing approximately one third of the sugar in the form of the ammonium aldonate[5]. This part is adsorbed on the column and lost during regeneration with NH_4Cl solution. Apart from this minor complication, the three step synthesis IIb is the reaction pathway of choice to prepare *O*-acetylated *N*-allylmaltoheptaonamide.

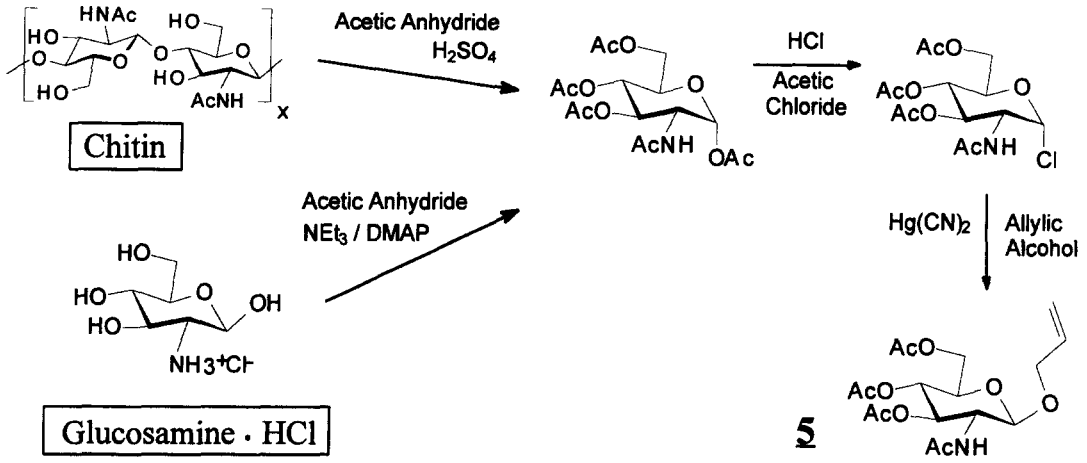
Hydrosilylation of O-acetylated N-allylaldonamides

Owing to the amide linkage of the carbohydrate derivatives $\mathbf{4_n}$, they cannot be hydrosilated using some of the more common transition metal catalysts such as Speier's catalyst ($H_2PtCl_6 \cdot 6H_2O$) or dicyclopentadienylplatinum(II)



Scheme 2

chloride[3]. As reported previously[4], bis-(1,5-cyclooctadiene)dirhodium(I) (Rh-COD) dichloride[6] is capable of catalysing the polymer-analogous addition of Si–H groups to pentaacetyl-*N*-allylgluconamide. From *Figure 1* it can be seen that no induction period occurs. Whereas the reaction proceeds up to quantitative addition in the case of gluconamide and the smaller polymer [Si 190/19] ($\overline{M_w}$ = 14 kg mol^{-1}), it was necessary to add an extra portion of catalyst in the case of the rather high molecular weight siloxane [Si 880/19] ($\overline{M_w}$ = 65 kg mol^{-1}) after several



Scheme 3

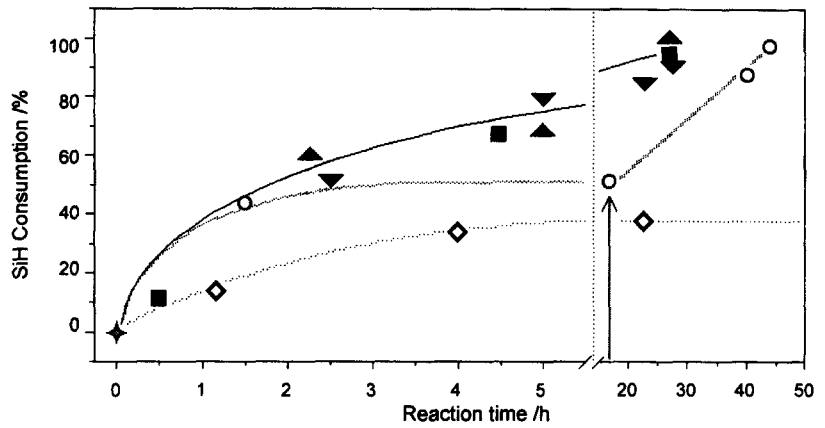


Figure 1 Hydrosilylation catalysed by bis-(1,5-COD)dirhodium(I) dichloride (each 1/100 molar); ■, ▲, ▼: Ac_5GlcA-N-allyl + [Si 190/19], several runs; ○: Ac_5GlcA-N-allyl + [Si 880/19]; arrow: after 17 h additional catalyst; ◇: $Ac_{23}Glc_7$A-N-allyl + [Si 880/19], stagnation at 40%

Table 3 Hydrosilylation by various catalysts[a,b]

	Catalyst						
Olefin	$(dCp)_2$-$PtCl_2$	H_2PtCl_6	$(NH_4)_2PtCl_4$	$Co_2(CO)_8$	$(Ph_3P)_2Rh(CO)Cl$	$(COD)_2Rh_2Cl_2$	$(R_2S)_2PtCl_2$
Allyl acetate	+	○	/	–	○	+	+
N-Allylacetamide	/	○	/	/	○	+	+
Ac_5GlcA-*N*-allyl	/	○	–	/	○	+	+
$Ac_{23}Glc_7$A-*N*-allyl	/	○	–	–	–	○	+

[a] Conditions: 250 mM olefinic compound, 200 mM Si–H as [Si 190/19] (if not otherwise stated in text), 1/1000–1/100 mol% of catalyst, solvent: toluene at 70°C under N_2.

[b] /, no formation of Si–C bonds; ○, limited hydrosilylation, large proportion of side reactions; +, hydrosilylation up to quantitative conversion of Si–H to Si–C; –, not investigated

hours. Using this catalyst, quantitative addition of maltoheptaonamide **4** failed; the reaction stopped after about 40% conversion. Addition of another portion of catalyst did not improve the efficiency.

The search for an appropriate catalyst became essential for establishing a suitable reaction sequence to synthesize aldonamide siloxanes. After testing a large set of other transition metal complexes in a non-carbohydrate model reaction with *N*-allylacetamide, we found that only bis(dialkylsulfido)platinum(II) salts are able to catalyse Si–C bond formation in the presence of amide structures. An overview is given in *Table 3*.

Using *cis*-bis(dialkylsulfido)platinum(II) chlorides, it was possible to add all the tested olefinic compounds quantitatively to both a rather short siloxane [Si 98/5] ($\overline{M_w}$ = 7.2 kg mol^{-1}) and the high molecular weight backbone [Si 880/19] ($\overline{M_w}$ = 65 kg mol^{-1}), no matter whether acetamide, a functionalized monosaccharide or the bulky maltoheptaonamide **4** was used. Varying the alkyl ligands of this complex, we found that ethyl- and benzylsulfido platinum salts catalyse hydrosilylation faster than methyl, isopropyl and phenyl sulfides (see *Table 4*). All other transition metal complexes afforded only poor, if any, hydrosilylation rates, and side reactions—such as reduction of C=C or C=O double bonds, or even Si–O–Si chain scission—became substantial in some cases (i.e. H_2PtCl_6).

Table 4 Degree of conversion of Si–H groups with different platinum sulfido-complexes after 52 h[a]

Ligand R in $(R_2S)_2PtCl_2$	Methyl	Ethyl	Isopropyl	Phenyl	Benzyl
Conversion/%	41	49	22	41	62

[a] Conditions: 1/2000 molar catalyst; Ac_5GlcA-*N*-allyl 1.2-fold according to [Si 540/23]; $T = 70°C$; solvent toluene

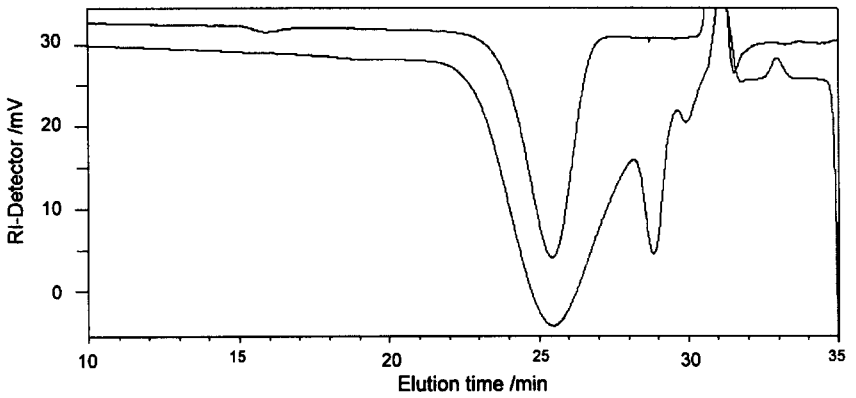


Figure 2 G.p.c. elution curve of $Ac_{23}Glc_7$A-N-[Si 98/5] on SDV-Gel, solvent toluene; top: pure aldonamide siloxane after purification by preparative GPC; bottom: reaction mixture, the product appearing at 25.5 min

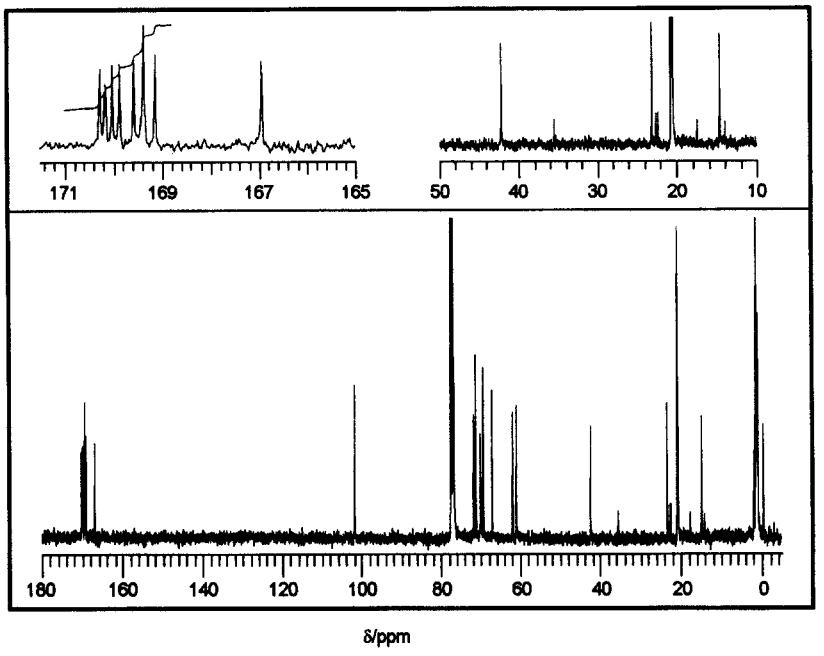


Figure 3 100 MHz ^{13}C n.m.r. ($CDCl_3$, δ/ppm) of Ac_8LacA-N-[Si 540/14]; 170.3–169.15: C=O acetate (8 C); 167.0: C-1 amide (1 C); 101.4: C-1′ (1 C); 77.4–68.1: C-2/3/4/5/2′/3′/4′/5′ (8 C); 61.8/60.9: C-6/6′ (2 × 1 C); 42.2: N–CH_2– (1 C); 23.1: –CH_2–propyl (1 C); 20.8–20.4: –CH_3 acetate (8 C); 14.6: –CH_2–Si propyl (1 C); 1.7– – 0.6 Si–CH_3; additional signals of pentyl capping: 35.5/22.6/22.3: –CH_2– (3 × 1 C); 17.4: –CH_2–Si (1 C); 13.9: –CH_3 (1 C)

From a g.p.c. elution curve (*Figure 2*) of the hydrosilylation product $Ac_{23}Glc_7$A-N-[Si 98/5] it can be seen that the maltoheptaonamide siloxane appears at the high molecular weight edge (25.5 min elution time), whereas low molecular weight byproducts (due to reduction of the allylamide structure) emerge at 29 and 30 min. These impurities are easily removed by preparative g.p.c.

In all cases hydrosilylation strictly follows anti-Markovnikov orientation, as demonstrated by ^{13}C DEPT and spin–echo n.m.r. spectroscopy[5]. Adding maltoheptaonamide **4** to [Si 540/23], quantitative conversion of Si–H to Si–C could not be achieved. This fact might have its reason in an amount of block-like structure of the hydromethylsiloxane units in [Si 540/23]. Thus, because of steric hindrance of bulky maltoheptaose, a maximum degree of conversion of only 75% could be achieved. The product is described as $Ac_{23}Glc_7$A-N-[Si 540/17], indicating that $\bar{n} = 17$ carbohydrate residues per chain (75% degree of conversion). In this case it was possible to cap the remaining Si–H groups in the presence of excess **4** by adding 1-pentene without the addition of further amounts of catalyst.

The platinum(II) complexes of ethylsulfido and benzylsulfido ligands allow the hydrosilylation reaction of gluconamide and maltoheptaonamide as well as those of galactose, maltose, cellobiose, lactobiose and the glucosamine derivative **5**. As an example, the ^{13}C n.m.r. spectrum of lactobionamide-modified siloxane Ac_8LacA-N-[Si 540/

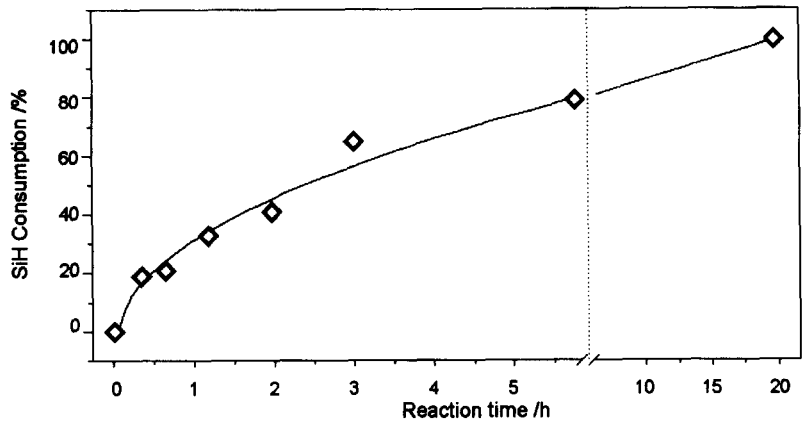


Figure 4 Hydrosilylation catalysed by $(Bn_2S)_2PtCl_2$ (1/200 molar) of *N*-allylacetamide and [Si 190/19], according to *FT*i.r. analysis

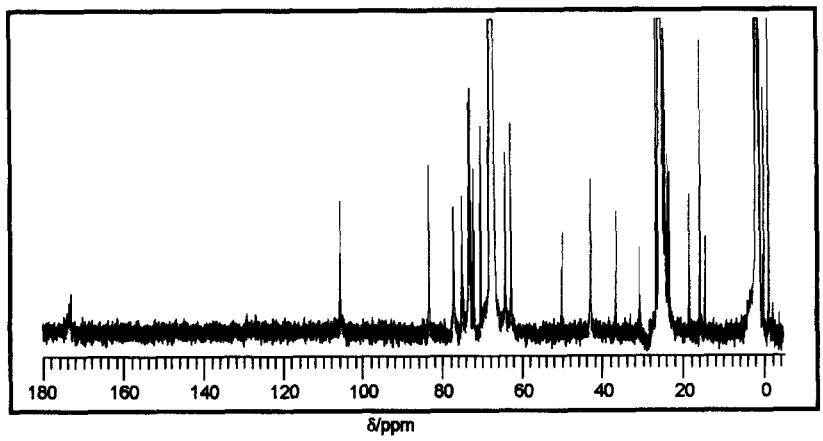


Figure 5 100 MHz ^{13}C n.m.r. (THF-d_8, 105 000 scans, δ/ppm) of LacA-N-[Si 540/14]; 173.0: C-1 amide; 105.6: C-1′; 83.2/77.1/74.9/73.2/73.1/72.7/72.0/70.1: C-2/3/4/5/2′/3′/4′/5′; 64.0/62.6: C-6/C-6′; 42.5: N-CH_2–; 36.3/26.2/23.4/23.1: –CH_2–; 18.2: –CH_2–Si pentyl; 15.4: –CH_2–Si propyl; 14.2: –CH_3 pentyl; 1.9– – 1.2: Si–CH_3 (50.4: methanol and 30.4: acetone)

14] is shown. Again the few remaining Si–H groups were capped by addition of 1-pentene (*Figure 3*).

The rate of the hydrosilylation reaction has been studied for the addition of *N*-allylacetamide to [Si 190/19], as shown in *Figure 4*. No induction period is observable in the reaction catalysed by *cis*-bis(dibenzylsulfido)platinum(II) chlorides $(Bn_2S)PtCl_2$ by analogy with the Rh-COD catalysed reaction. The platinum salt remains active until quantitative Si–H conversion is achieved if the steric requirements of the olefinic compound allow this. The efficiency of this class of hydrosilylation catalysts has been checked for other highly functional olefins[7].

We have observed that the spatial requirements of catalyst *and* olefinic compound *and* siloxane determine the maximum degree of conversion of Si–H to Si–C in the polymer-analogous hydrosilylation reaction. If the olefinic moiety is comparatively small (*N*-allylacetamide or penta-acetyl-*N*-allylgluconamide), quantitative turnover can be attained with either ethyl- or benzylsulfido ligands, and the benzylsulfido complex adds Si–H faster to C=C. Starting from bulky maltoheptaonamide **4**, a high degree of conversion was possible using solely the ethylsulfido complex and either a rather short siloxane backbone [Si 98/5], or [Si 880/19] having a low amount of Si–H groups (2 mol%). The lowest maximum degree of conversion was found using the benzylsulfido catalyst, maltoheptaonamide **4**, and [Si 540/23], where approximately 25% of the Si–H groups are present in a block-like structure. Attempts at steric decoupling of maltoheptaose from the terminal C=C double bond, using decenyl instead of allyl spacers, failed. In this case, the maximum degree of conversion was in the range of only 34–40% for [Si 260/12] and [Si 540/23].

An overview of aldonamide siloxanes synthesized by this method is given in *Table 5*. Deprotection of the OH groups was achieved as described prevously[5] by two methods, transesterification by $MeOH/K_2CO_3$ or by MeOH/KCN. The latter reagents give rise to fewer side reactions. The resulting aldonamide siloxanes (''sweet siloxanes'') are summarized in *Table 6*.

The ^{13}C n.m.r. spectrum of *O*-deprotected LacA-N-[Si 540/14] is shown in *Figure 5* as a typical representative of this class of materials. Because of the large number of scans necessary, and a small drift of the magnetic field during data acquisition over three days, any quantitative interpretation of the peaks intensities had to be abandoned.

The solubility behaviour of aldonamide siloxanes has proved quite surprising. *Table 7* summarizes the solubility characteristics of sweet siloxanes containing [Si 540/23] ($\overline{M}_w$ = 40 kg mol^{-1}) as a backbone of medium molecular weight. Some surprising features of the solution behaviour are:

- Gluconamide siloxane (GlcA-) can be dissolved only in THF in low concentrations, whereas THF is actual a good solvent for PDMS alone as well as for gluconic acid derivatives.

Table 5 *O*-Acetylated aldonamide siloxanes synthesized by hydrosilylation with $(R_2S)_2PtCl_2$

Siloxane	Saccharide	Conv., time	Cat.[a] conc./ mol% SiH	Characterization
[Si 98/5]	$Ac_{23}Glc_7A$-*N*-allyl (in THF)	100% 18 h	Ethyl 1.1	I.r.: 3474/3396(w): νN–H; 2962(s): νC–H; 1750(s): νC=O acetate; 1686(w): νC=O amide I; 1528(w): νN–H amide II; 1372(s): δC–H; 1260(s): δSi–C; 1230/1084/1036(b): νC–O/νSi–O; 802(s): νSi–C; ^{13}C n.m.r. (50 MHz): 170.98–169.14: C=O acetate; 166.39: C-1 amide; 97.48: C^{II}-1; 95.62: C^{chain}-1; 73.55–67.91: C/2/3/4/5; 62.38–61.38: C-6; 42.19: N–CH_2–; 22.99: –CH_2–; 21.06–20.55: –CH_3 acetate; 14.48: –CH_2–Si; 1.74– – 0.63: Si–CH_3
[Si 540/23]	$Ac_{23}Glc_7A$-*N*-allyl (in THF)	74% 21 h	Ethyl 1.0	I.r.: identical to above; ^{13}C n.m.r.: (100 MHz; spin–echo): identical to above, additional signals of pentyl residues:35.7/22.5/22.7: –CH_2– (3 × 1 C); 17.5: –CH_2–Si (1 C); 14.1: –CH_3 (1 C)
[Si 540/23]	$Ac_{23}Glc_7A$-*N*-allyl	65% 190 h	Ethyl 0.1	I.r.: identical to above; ^{13}C n.m.r. (100 MHz): identical to above
[Si 540/23]	$Ac_{23}Glc_7A$-*N*-allyl	65% 120 h	Benzyl 0.27	^{13}C n.m.r. (100 MHz): identical to above
[Si 880/19]	$Ac_{23}Glc_7A$-*N*-allyl (in THF)	100% 19 h	Ethyl 1.0	I.r.: identical to above. Signals of saccharides appear with less intensity
[Si 260/12]	$Ac_{23}Glc_7A$-*N*-$C_{10}H_{19}$	34% 86 h	Benzyl 0.27	IR: identical to above; ^{13}C n.m.r. (100 MHz): 170.80–169.15: C=O acetate; 166.42: C-1 amide (1 C); 97.47–95.73: $C^{II–VII}$-1; 73.81–68.16: C-2/3/4/5; 62.61–61.54: C-6; 39.55: N–CH_2– (1 C); 33.33–22.99: –CH_2– (8 C); 20.97–20.49: –CH_3 acetate; 17.53: –CH_2–Si (1 C); 1.36–0.63: Si–CH_3
[Si 540/23]	$Ac_{23}Glc_7A$-*N*-$C_{10}H_{19}$	40% 86 h	Benzyl 0.27	I.r. and ^{13}C n.m.r.: identical to above
[Si 540/23]	Ac_5GlcA-*N*-allyl	91% 20 h	Ethyl 0.5	I.r.: 3366(w): νN–H; 2262(s): νC–H; 1756(s): νC=O acetate; 1684(w): νC=O amide I; 1534(w): δN–H amide II; 1372(s): δCH_3; 1262(s): δSi–C; 1094/1024(b): νC–O/νSi–O; 802(s): νSi–C ^{13}C n.m.r. (100 MHz): 170.49/169.79/169.70/169.45/169.05: C=O acetate (6 × 1 C); 165.91: C-1 amide (1 C); 71.71/69.54/69.24/68.92: C-2/3/4/5 (4 × 1 C); 61.61: C-6 (1 C); 42.26: N–CH_2– (1 C); 23.13: –CH_2– (1 C); 20.68/20.59/20.36: –CH_3 acetate (5 C); 14.58: –CH_2–Si (1 C); 1.75– – 0.58: Si–CH_3
[Si 540/23]	Ac_5GlcA-*N*-allyl	86% 42 h	Benzyl 0.2	I.r.: identical to above; ^{13}C n.m.r. (100 MHz): identical to above
[Si 260/12]	Ac_5GlcA-*N*-allyl	92% 96 h	Benzyl 0.2	I.r.: identical to above; ^{13}C n.m.r. (100 MHz): identical to above
[Si 540/23]	Ac_5GlcA-*N*-allyl	77% 120 h	Benzyl 0.27	I.r.: identical to above; ^{13}C n.m.r. (100 MHz): identical to above
[Si 540/23]	Ac_5GalA-*N*-allyl	76% 120 h	Benzyl 0.27	I.r.: similar to that of gluconamide siloxane ^{13}C n.m.r. (100 MHz): 170.40/169.83/169.27/168.36: C=O acetate (5 C); 166.11: C-1 amide; 71.06/68.01/67.54/67.42: C-2/3/4/5 (4 × 1 C); 62.10: C-6 (1 C); 42.13: N–CH_2– (1 C); 23.18: –CH_2– (1 C); 20.72/20.68/20.59/20.53/20.38: –CH_3 acetate (5 C); 14.49: –CH_2–Si (1 C); 1.74– – 0.61: Si–CH_3
[Si 540/23]	Ac_8MalA-*N*-allyl	73% 120 h	Benzyl 0.27	I.r.: similar to that of gluconamide siloxane; ^{13}C n.m.r. (100 MHz): 170.71/170.49/170.38/169.89/169.64/169.54/169.43/169.05: C=O acetate (8 × 1 C); 166.35: C-1 amide (1 C); 97.69: C-1′ (1 C); 76.84/71.51/71.12/71.04/70.32/69.90/68.41/68.28: C-2/3/4/5/2′/3′/4′/5′ (8 × 1 C); 62.48/61.74: C-6/6′ (2 × 1 C); 42.24: N–CH_2– (1 C); 23.11: –CH_2– (1 C); 20.89–20.61: –CH_3 acetate (8 C); 14.57: –CH_2–Si (1 C); 1.78– – 0.64: Si–CH_3
[Si 540/23]	Ac_8CelA-*N*-allyl	73% 120 h	Benzyl 0.27	^{13}C n.m.r. (100 MHz): 170.62/170.27/170.09/169.58/169.49/169.28/169.09: C=O acetate (8 C); 167.04: C-1 amide (1 C); 101.37: C-1′ (1 C); 77.40/73.17/72.00/71.64/71.18/69.81/69.05/68.07: C-2/3/4/5/2′/3′/4′/5′ (8 × 1 C); 61.81/61.27: C-6/6′ (2 × 1 C); 42.20: N–CH_2– (1 C); 23.07: –CH_2– (1 C); 20.74–20.54: –CH_3 acetate (8 C); 14.58: –CH_2–Si (1 C); 1.72– – 0.62: Si–CH_3
[Si 540/23]	Ac_8LacA-*N*-allyl	60% 120 h	Benzyl 0.27	^{13}C n.m.r. (100 MHz): 170.27/170.17/170.03/169.88/169.58/169.38/169.15: C=O acetate (8 C); 166.95: C-1 amide (1 C); 101.68: C-1′ (1 C); 71.63/71.10/71.06/69.91/69.31/69.20/66.90: C-2/3/4/5/2′/3′/4′/5′ (8 C); 61.79/60.85: C-6/6′ (2 × 1 C); 42.20: N–CH_2– (1 C); 23.10: –CH_2– (1 C); 20.75–20.42: –CH_3 acetate (8 C); 14.57: –CH_2–Si (1 C); 1.73– – 0.61: Si–CH_3; additional signals of pentyl: 35.45/22.56/22.29: –CH_2– (3 × 1 C); 17.41: –CH_2–Si (1 C); 13.89: –CH_3 (1 C)
[Si 540/23]	$Ac_3GlcNAc$-1-*O*-allyl	99% 90 h	Benzyl 0.27	I.r.: 3284(w): νC–H; 2962(s): νC–H; 1748(s): νC=O acetate; 1658(s): νC=O amide I; 1560(w): δN–H amide II; 1412/1372(w): δC–H; 1260(s): δSi–C; 1094/1024(b): νSi–O/νC–O; 802(s): νSi–C
[Si 1500/12]	$Ac_3GlcNAc$-1-*O*-allyl	95% 90 h	Benzyl 0.27	I.r.: identical to above. Signals of saccharides appear with lower intensity

[a] Indicates ligand –R.

- Disaccharide siloxanes (MalA-, CelA-, and LacA-) are soluble in both toluene (a precipitating agent for saccharides) and isopropanol, which is a poor solvent for unprotected carbohydrates and also a precipitating agent for PDMS. The uptake in petroleum ether is very small, even though this liquid is a good solvent for pure dimethylsiloxanes.
- Chito-siloxane (PDMS modified by *N*-acetylglucosamine, GlcNAc-), on the other hand, is soluble only in petroleum ether or THF.
- Maltoheptaonamide siloxane (Glc_7A-) is the only one of the group which exhibits affinity for water. A stable aqueous suspension of this material can be formed.

Table 6 "Sweet siloxanes" of various carbohydrates

Product	Method of deprotection	Characterization
GlcA-N-[Si 190/19]	K_2CO_3	I.r. 3400(b): νO–H; 2966(s): νC–H; 1658(w): νC=O amide I; 1548(w): δN–H amide II; 1414(s): δC–H; 1262(s): δSi–C; 1098/1022(b): νC–O/νSi–O; 800(s): νSi–C
GlcA-N-[Si 260/11]	KCN	I.r.: identical to above
GlcA-N-[Si 540/17]	KCN	I.r.: identical to above; ^{13}C n.m.r. (100 MHz; THF-d_8): 172.75: C-1 amide; 74.61/74.07/72.82/72.08: C-2/3/4/5; 64.91: C-6; 42.44: N–CH_2–; 24.15: –CH_2–; 15.41: –CH_2–Si; 1.82– – 1.52: Si–CH_3
Glc_7A-N-[Si 62/4]	K_2CO_3	I.r.: 3366(b): νO–H; 2962(s): νC–H; 1652(s): νC=O amide I; 1540(w): δN–H amide II; 1412(s): δC–H; 1260(s): δSi–C; 1088/1020(b): νC–O/νSi–O; 800(s): νSi–C
Glc_7A-N-[Si 98/5]	K_2CO_3	I.r.: identical to above
Glc_7A-N-[Si 540/17]	KCN	I.r.: identical to above; ^{13}C n.m.r. (100 MHz; DMF-d_7): 172.93: C-1 amide; 102.19: C^{chain}-1; 81.37–71.47: C-2/3/4/5; 63.87–61.64: C-6; 42.23: N–CH_2–; 22.88: –CH_2–; 14.39: –CH_2–Si; 2.13– – 0.30: Si–CH_3
Glc_7A-N-[Si 540/15]	KCN	I.r.: identical to above
Glc_7A-N-[Si 880/19]	KCN	I.r.: identical to above. Signals of saccharides with lower intensity
GalA-N-[Si 540/17]	KCN	I.r.: similar to that of gluconamide siloxane; ^{13}C n.m.r. (100 MHz; THF-d_8): 173.83: C-1 amide; 72.44/72.08/71.37/68.07: C-2/3/4/5; 65.21: C-6; 42.48: N–CH_2–; 15.41: –CH_2–Si; 1.24– – 1.51: Si–CH_3
MalA-N-[Si 540/17]	KCN	I.r.: similar to that of gluconamide siloxane; ^{13}C n.m.r. (100 MHz; THF-d_8): 171.79: C-1 amide; 101.03: C-1′; 83.26/74.19/73.21/72.71/72.11/72.01/70.87/67.07: C-2/3/4/5/2′/3′/4′/5′; 62.99/61.85: C-6/C-6′; 41.59: N–CH_2–; 23.25: –CH_2–; 14.44: –CH_2–Si; 0.84– – 2.50: Si–CH_3
CelA-N-[Si 540/17]	KCN	I.r.: similar to that of gluconamide siloxane
LacA-N-[Si 540/14]	KCN	I.r.: similar to that of gluconamide siloxane; ^{13}C n.m.r. (100 MHz; THF-d_8): 173.02: C-1 amide; 105.56: C-1′; 83.24/77.05/74.85/73.18/73.06/72.76/72.02/70.09: C-2/3/4/5/2′/3′/4′/5′; 63.98/62.60: C-6/C-6′; 42.53: N–CH_2–; 36.31/26.20/23.44/23.07: –CH_2–; 18.17: –CH_2–Si pentyl; 15.43: –CH_2–Si propyl; 14.23: –CH_3 pentyl; 1.85– – 1.19: Si–CH_3
GlcNAc-1-O-[Si 540/23]	KCN	I.r.: 3412(b): νO–H; 2962(s): νC–H; 1652(s): νC=O amide I; 1560(w): δN–H; 1414(w): δC–H; 1260(s): δSi–C; 1094/1024(b): νSi–O/νC–O; 802(s): νSi–C ^{1}H n.m.r. (200 MHz; THF-d_8): 2.42(s): –CH_3 acetamide (69 H); 0.46(m): –CH_2–Si (46 H); 0.00(s): Si–CH_3 (set to 3200 H); ^{13}C n.m.r. (50 MHz; THF-d_8): 170.85: C=O acetamide; 101.72: C-1; 77.55/76.44/71.96: C-3/4/5; 70.85: 1-O–CH_2–; 63.16: C-6; 58.29:C-2; 30.64: –CH_2–; 23.18: –CH_3 acetamide; 14.31: –CH_2–Si;2.13– – 1.35: Si–CH_3
GlcNAc-1-O-[Si 1500/12]	KCN	I.r.: identical to above. Signals of saccharides with lower intensity

Table 7 Some solubility characteristics of aldonamide siloxanes[a]

Aldonamide siloxane	Solvent				
	Petroleum ether	Toluene	THF	Isopropanol	Water
GlcA-N-[Si 540/17]	W 1.7	W 5	S 20	W 6	×
GalA-N-[Si 540/17]	W 4	J 12	S 40	J 20	×
MalA-N-[Si 540/17]	W 0.2	S 40	S 40	S 40	×
CelA-N-[Si 540/17]	W 0.2	S 40	S 20	S 40	×
LacA-N-[Si 540/14]	W 0.6	S 40	S 20	S 40	×
GlcNAc-1-O-[Si 540/23]	S 40	–	S 40	W 1.7	×
Glc_7A-N-[Si 540/15]	×	×	S 10	W 0.5	W 0.5; P 7

[a] S *n*: soluble, maximum of investigated concentration ≈ *n* mg ml^{-1}.
W *n*: swelling by *n*-fold uptake of solvent, gel formation.
J *n*: formation of jelly by *n*-fold uptake of solvent.
P *n* : formation of suspension, stable up to ≈ *n* mg ml^{-1}.
× : insoluble, no uptake of solvent.
–: not investigated.

EXPERIMENTAL

General

All solvents of p.a. grade and carbohydrates were purchased from Fluka. *FT*i.r. spectra were recorded with a Bruker IFS-48 spectrometer and n.m.r. spectra were taken on a Bruker AM-400 instrument. Potato phosphorylase, glucose 1-phosphate, and maltoheptaose **1** were prepared and characterized as described in a previous publication[4].

The i.r. and n.m.r. spectra of the intermediates and the final products are summarized in *Table 8* and *Table 9*.

Reactions according to path a, Scheme 2

β-Peracetylated carbohydrates. Preparation using acetic anhydride and sodium acetate was carried out using the standard procedure of Wolfrom and Thompson[4,8], irrespective of the carbohydrate involved. Yields were in the range 50–60% after purification by chromatography. In the case of galactose and cellobiose the β-peracetylated carbohydrates were purchased from Fluka.

1-OH deprotected carbohydrates. Deacetylation of the anomeric oxygen was achieved according to Excoffier et al.[9] by hydrazinolysis at 60°C. In the case of cellobiose acetate only, it was necessary to dissolve Ac_8Cel at 100°C in DMF at a concentration of 25% by weight.

Peracetylated aldonic acid lactones. Oxidation of the anomeric lactol group was carried out as described previously[4] by treatment with DMSO and acetic anhydride[10], but with a minor change in the order of adding the reagents: DMSO and acetic anhydride were mixed first to form the true oxidizing compound, *SS*-dimethyl(*O*-acetyl)sulfonium acetate. This mixture was added after 1 h to the solution of the 1-OH deprotected carbohydrate acetate in DMSO.

Table 8 Carbohydrate derivatives obtained according to path a in *Scheme 2*

Substrate	Reaction			
	1-OH deprotection	Oxidation	Amide formation	5-OH acetylation
Gal: Yield[a]; MP[b]; R_f[c]	62%; syrup0.29 (3:1) I.r.: 3454(s): νO–H; 2974(w): νC–H; 1750(s): νC=O acetate; 1230/1054(b): νC–O^{13}C n.m.r.: 170.59–170.09: C=O acetate; 95.49/90.25: α/β C-1 (2 × 1 C); 70.61/70.53/70.44/68.27/68.04/67.14/67.03/65.72: α/β C-2/3/4/5 (8 × 1 C); 61.57/61.30: α/β C-6 (2 × 1 C); 20.57–20,43: –CH_3 acetate	87%; syrup[f] I.r.[d]: 2940(w): νC–H; 1750(s): νC=O acetate/lactone, 1220/1090(b): νC–O^{13}C n.m.r.[e]: 169.92/169.4/169.48/169.23: C=O acetate (4 × 1 C); 164,72: C-1 lactone (1 C); 74.59/69.03/68.27/66.20: C-2/3/4/5 (4 × 1 C); 60,88: C-6 (1 C); 20.23/20.21/20.11/20.08: –CH_3 acetate (4 × 1 C)	47%; 164°C; 0.18 (2:1) ^{13}C n.m.r.: 170.62/170.23/169.66/169.03: C=O acetate (4 × 1 C); 167.39: C-1 amide (1 C); 133,44: –CH= allyl (1 C); 116.98: =CH_2 allyl (1 C); 72.38/70.13/69.08/68.60: C-2/3/4/5 (4 × 1 C); 63,04: C-6 (1 C); 41.88: N–CH_2– allyl (1 C); 20.55–20.37: –CH_3 acetate (4 C)	63%; 144°C; 0.42 (2:1) ^{13}C n.m.r.: 170.27/170.19/169.64/169.39/168.46: C=O acetate (5 × 1 C); 166.14: C-1 amide (1 C); 133.45: –CH= allyl (1 C); 116.89: =CH_2 allyl (1 C); 71.06/68.03/67.52/67.41: C-2/3/4/5 (4 × 1 C); 61.95: C-6 (1 C); 41.67: N–CH_2– allyl (1 C); 20.59/20.55/20.47/20.39/20.30: –CH_3 acetate (5 × 1 C)
Mal: Yield; MP; R_f	79%; 172°C; 0.32 (3:1) ^{13}C n.m.r.: 170.50/170.46/170.42/170.28/170.13/169.95/169.77/169.31: C=O acetate; 95.47/95.42/94.69/89.78: α/β C-1/1′ (4 × 1 C); 74.92/73.65/72.80/72.27/71.57/69.95: α/β C-2/3/4/5/2′/3′/4′/5′; 62.86/62.80/61.45/61.40: α/β C-6/6′ (4 × 1 C); 20.75–20.36: –CH_3 acetate	97%; 135°C[f] ^{13}C n.m.r.: 170.09/170.03/169.89/169.73/169.50/169.20/169.08: C=O acetate (7 × 1 C); 164.10: C-1 lactone (1 C); 96.09: C-1′; 72.91/71.53/69.90/69.07/69.00/68.54/68.22/67.95: C-2/3/4/5/2′/3′/4′/5′; (8 × 1 C); 62.42/61.62: C-6/6′ (2 × 1 C); 20.42/20.32/20.26/20.19/20.02: –CH_3 acetate (7 C)	19% (impure syrup)0.30 (3:1) I.r.: 3394(s): νN–H/νO–H; 3086(w): νH–C= allyl; 2960(w): νC–H; 1750(s): νC=O acetate; 1684(s): νC=O amide I; 1534(w): δN–H amide II; 1224/1040(s): νC–O	Not synthesized according to *Scheme 2* path a.
Cel: Yield; MP; R_f	76%; 197°C; 0.25 (3:1) I.r.: 3290(b): νN–H/νO–H; 2920(w): νC–H; 1650(s): νC=O amide I; 1550(w): δN–H amide II; 1044(b): νC–O^{13}C n.m.r.: 170.34/170.25/170.16/170.01/169.97/169.54/169.50/469.10/168.87/168.85: C=O acetate; 100.48: C-1′ (1 C); 100.38/94.87: α/β C-1 (2 × 1 C); 89.72/76.31/76.24/73.09/72.84/72.77/72.74/72.04/71.69/71.52/71.29/69.27/67.91/67.82/67.76: α/β C-2/3/4/5/2′/3′/4′/5′; 61.85/61.72: α/β C-6 (2 × 1 C); 61.50: C-6′ (1 C); 20.56–20.22: –CH_3 acetate	91%; 122°C[f] ^{13}C n.m.r.: 170.37/170.07/169.95/169.54/169.19/168.96: C=O acetate (7 C); 164.51: C-1 lactone (1 C); 100.51: C-1′ (1 C); 76.04/74.34/72.62/72.00/71.26/70.10/69.93/67.64: C-2/3/4/5/2′/3′/4′/5′ (8 × 1 C); 61.44/61.32: C-6/6′ (2 × 1 C); 20.62–20.22: –CH_3 acetate	9%; 110°C; 0.20 (2:1) I.r.: 3478(s): νN–H; 3390(s): νO–H; 3080(w): νH–C= allyl; 2942(w): νC–H; 1752(s): νC=O acetate; 1687(s): νC=O amide I; 1532(w): δN–H amide II; 1228/1040(b): νC–O^{13}C n.m.r.: 170.91/170.70/170.35/169.99/169.23/169.21/169.16: C=O acetate (7 × 1 C); 166.96: C-1 amide (1 C); 133.38: –CH= allyl (1 C); 116.54: =CH_2 allyl (1 C); 101.38: C-1′ (1 C); 78.89/73.05/71.85/71.61/71.54/69.96/69.44/67.97: C-2/3/4/5/2′/3′/4′/5′ (8 × 1 C); 64.98: C-6 (1 C); 61.33: C-6′ (1 C); 41.54: N–CH_2– allyl (1 C); 20.66–20.38: –CH_3 acetate (7 C)	88%; 124°C; 0.38 (2:1) I.r.: 3424(s): νN–H; 3086(w): νH–C= allyl; 2952(w): νC–H;1752(s): νC=O acetate; 1682(s): νC=O amide I; 1530(w): δN–H amide II; 1224/1046(s): νC–O^{13}C n.m.r.: 170.75/170.48/170.32/169.84/169.60/169.55/169.38/169.29: C=O acetate (8 × 1 C); 166.45: C-1 amide (1 C); 133.36: –CH= allyl (1 C); 116.52: =CH_2 allyl (1 C); 101.31: C-1′ (1 C);77.32/72.96/71.81/71.45/71.02/69.63/68.90/67.81: C-2/3/4/5/2′/3′/4′/5′ (8 × 1 C); 61.63: C-6 (1 C); 61.21: C-6′ (1 C); 41.58: N–CH_2– allyl (1 C); 20.86–20.44: –CH_3 acetate
Lac: Yield; MP; R_f	93%; 84°C; 0.18 (3:1) I.r.: 3470(s): νO–H; 2978/2876 (w): νC–H; 1750(s): νC=O acetate; 1230/1058(s): νC–O^{13}C n.m.r.: 170.11/169.90/169.55/169.30/168.67: C=O acetate; 100.17: C-1′ (1 C); 94.06/89.13: α/β C-1 (2 × 1 C); 75.67/72.16/70.87/70.40/69.87/69.13/68.60/67.33/66.34: α/β C-2/3/4/5/2′/3′/4′/5′; 61.63/60.49: C-6/6′ (2 × 1 C); 20.11–19.87: –CH_3 acetate	63%; 148°C; 0.34, tailing (3:1) ^{13}C n.m.r.: 169.89/169.70/169.67/169.54/169.23/168.89/168.66: C=O acetate (7 × 1 C); 164.38: C-1 lactone (1 C); 100.42: C-1′ (1 C); 75.85/73.68/70.38/69.99/69.44/68.44/66.45: C-2/3/4/5/2′/3′/4′/5′ (8 C); 61.19/60.62: C-6/6′ (2 × 1 C); 20.18–19.82: –CH_3 acetate	45%; 51°C; 0.29 (2:1) ^{13}C n.m.r.: 170.91/170.28/170.23/170.00/169.81/169.37/169.31: C=O acetate (7 × 1 C); 166.95: C-1 amide (1 C); 133.42: –CH= allyl (1 C); 116.59: =CH_2 allyl (1 C); 101.75: C-1′ (1 C); 78.93/71.99/71.01/70.91/70.18/69.52/69.12/66.99: C-2/3/4/5/2′/3′/4′/5′ (8 × 1 C); 65.00: C-6 (1 C); 60.95: C-6′ (1 C); 41.55: N–CH_2– allyl (1 C); 20.65–20.31: –CH_3 acetate	90%; 75°C; 0.31 (2:1) I.r.: 3384(s): νN–H; 3082/3030 (w): νH–C=; 2968/2878(w): νC–H; 1750(s): νC=O acetate; 1680(s): amide I; 1530(w): δN–H amide II; 1222/1050(s): νC–O^{13}C n.m.r.: 170.21/169.94/169.80/169.50/169.40/169.08: C=O acetate (8 C); 166.91: C-1 amide (1 C); 133.43: –CH= allyl (1 C); 116.51: =CH_2 (1 C); 101.58: C-1′ (1 C); 77.11/71.44/70.96/70.92/69.79/69.20/69.02/66.83: C-2/3/4/5/2′/3′/4′/5′ (8 × 1 C); 61.61: C-6 (1 C); 60.87: C-6′ (1 C); 41.49: N–CH_2– allyl (1 C); 20.61–20.28: –CH_3 acetate

Table 8 Continued

Substrate	Reaction			
	1-OH deprotection	Oxidation	Amide formation	5-OH acetylation
Glc_7: Yield; MP; R_f	81%; 123°C; 0.18 (2:1) I.r.: 3478(s): νO–H; 2962(s): νC–H; 1746(s): νC=O acetate; 1232/1034(b): νC–O^{13}C n.m.r.: 170.13–168.94: C=O acetate; 95.5: C^{chain}-1; 94.25/89.37: α/β-C^{I}-1; 74.81–67.10: C-2/3/4/5; 62.91–61.19: C-6; 20.33–20.03: –CH_3 acetate	91%; 115°C; 0.24, tailing (2:1) I.r.: 2962(w): νC–H; 1750(s): νC=O; 1240/1036(s): νC–O^{13}C n.m.r.: 170.29–168.93: C=O acetate; 164.09: C-1 lactone; 95.91: C^{II}-1; 95.49: C^{chain}-1; 78.39–67.88: C-2/3/4/5; 62.65-61.29: C-6; 20.52–19.97: –CH_3 acetate	83%; 125°C; 0.13 (3:2) I.r.: 3472/3394(w): νN–H/νO–H; 3020(w): νH–C= allyl; 2960(w): νC–H; 1750(s): νC=O acetate; 1684(w): νC=O amide I; 1526(w): δN–H amide II; 1236/1036(s): νC–O^{1}H n.m.r.: 6.26(t): –CH= allyl (1 H); 5.77(m): =CH_2 allyl; 5.53–3.83(m): H-1–6. NH–CH_2– allyl. –OH (44 H); 2.18–1.95: –CH_3 acetate (66 H) ^{13}C n.m.r.: 170.96–169.27: C=O acetate; 166.41: C-1 amide (1 C); 133.30: –CH= allyl (1 C); 116.45: =CH_2 allyl (1 C); 97.47: C^{II}-1; 95.50: C^{chain}-1; 78.47...67.74: C-2/3/4/5; 62.99–61.19: C-6; 41.45: N–CH_2– allyl (1 C); 20.66–20.36: –CH_3 acetate	81%; 121°C; 0.20 (3:2) I.r.: 3478/3390(w): νN–H; 3020(w): νH–C= allyl; 2960(w): νC–H; 1750(s): νC=O acetate; 1686(w): νC=O amide I; 1526(w): δN–H amide II; 1236/1036(s): νC–O^{13}C n.m.r.: 170.78–169.23: C=O acetate; 166.25: C-1 amide; 133.27: –CH= allyl; 116.47: =CH_2 allyl; 97.25: C^{II}-1; 95.52: C^{chain}-1; 76.69–67.74: C-2/3/4/5 (from this: 73.09/71.51/70.25/68.72: C^{chain}-2/3/4/5); 62.24: C^{chain}-6; 61.17: C^{I}-6; 41.48: N–CH_2– allyl; 20.87–20.36: –CH_3 acetate

[a] Yield in per cent of theoretical amount.
[b] MP, melting points uncorrected.
[c] R_f: solvent: toluene/acetone, ratio (v/v) given in brackets.
[d] *FT*i.r.: wavenumbers in cm^{-1}.
[e] N.m.r.: 400 MHz (^{1}H); 100 MHz (^{13}C), $CDCl_3$, δ in ppm.
[f] R_f not detectable owing to decomposition on silica.

Table 9 Carbohydrate derivatives obtained according to path b in *Scheme 2*

Substrate	Reaction		
	Oxidation	Amide formation	Peracetylation
Glc: Yield[a]; MP	Purchased from Fluka	78%; 118°C I.r.: 3512(s): νN–H; 3328(b): νO–H; 3082(w): νH–C= allyl; 2912(w): νC–H Glc; 1654(s): νC=O amide I; 1534(w): δN–H amide II; 1098(b): νC–O; ^{13}C n.m.r.: 174.13: C-1 amide (1 C); 133.21: =CH– allyl (1 C); 115.31: =CH_2 allyl (1 C); 73.34/72.11/70.94/70.17: C-2/3/4/5 (4 × 1 C); 62.47: C-6 (1 C); 41.07: N–CH_2– allyl (1 C)	46%; 147°C I.r.: 3254(s): νN–H; 3064(w): νH–C= allyl; 2938(w): νC–H Glc; 1750(s): νC=O acetate; 1656(s): νC=O amide I; 1554(w): δN–H amide II; 1226/1058(s): νC–O; ^{13}C n.m.r.: 170.50/169.76/169.56/169.11: C=O acetate (5 C); 165.90: C-1 amide (1 C); 133.37: =CH– allyl (1 C); 116.81: =CH_2 allyl (1 C); 71.58/69.34/69.04/68.75: C-2/3/4/5 (4 × 1 C); 61.47: C-6 (1 C); 41.70: N–CH_2– allyl (1 C); 20.63/20.57/20.33: –CH_3 acetate (5 C)
Gal: Yield; MP; R_f (solvent)	99.8%[f,g] I.r.: 3344(b): νO–H; 2940: νC–H; 1776(s): νC=O lactone; 1110(b): νC–O; ^{13}C n.m.r.: 175.80: C-1 lactone (1 C); 79.86/73.53/72.66/68.77: C-2/3/4/5 (4 × 1 C); 61.84: C-6 (1 C)	45%; 179°C0.76 (AcOEt/EtOH/H_2O 3:3:1) I.r.: 3290(b): νN–H/νO–H; 2920(w): νC–H; 1650(s): νC=O amide I; 1550 (w): δN–H amide II; 1044(b): νC–O; ^{13}C n.m.r.: 173.62: C-1 amide (1 C); 135.44: =CH– allyl (1 C); 115.08: =CH_2 allyl (1 C); 71.18/71.03/69.97/69.38: C-2/3/4/5 (4 × 1 C); 63.35: C-6 (1 C); 40.77: N–CH_2– allyl (1 C)	63% [h]
Mal: Yield; MP; R_f (solvent)	97%; 87°C[g] I.r.: 3400(b): νO–H; 2932(w): νC–H; 1740(s): νC=O lactone; 1022(b): νC–O; ^{13}C n.m.r.: 175.38: C-1 lactone (1 C); 100.25: C-1′ (1 C); 81.38/72.71/72.26/72.00/71.72/71.45/70.93/69.12: C-2/3/4/5/2′/3′/4′/5′ (8 × 1 C); 61.89: C-6 (1 C); 60.18: C-6′ (1 C)	72%; 70°C0.91 (acetone/MeOH/H_2O 2:1:1) I.r.: 3380(b): νN–H/νO–H; 2930(w): νC–H; 1650(s): νC=O amide I; 1544 (w): δN–H amide II; 1026(b): νC–O; ^{13}C n.m.r.: 174.10: C-1 amide (1 C); 133.25: –CH= allyl (1 C); 115.32: =CH_2 allyl (1 C); 100.36: C-1′ (1 C); 81.87/72.77/72.29/72.12/71.72/71.56/71.48/69.18: C-2/3/4/5/2′/3′/4′/5′ (8 × 1 C); 61.99: C-6 (1 C); 60.24: C-6′ (1 C); 41.11: N–CH_2– allyl (1 C)	49%; 66°C0.40 (toluene/acetone 2:1) ^{13}C n.m.r.: 170.72/170.46/170.38/169.86/169.64/169.57/169.40/169.27: C=O acetate (8 × 1 C); 166.40: C-1 amide (1 C); 133.45: –CH= allyl (1 C); 116.66: =CH_2 allyl (1 C); 97.58: C-1′; 76.70/71.50/71.00/70.93/70.25/69.78/68.33/68.23: C-2/3/4/5/2′/3′/4′/5′ (8 × 1 C); 62.30: C-6 (1 C); 61.69: C-6′ (1 C); 41.61: N–CH_2– allyl (1 C); 20.81–20.52: –CH_3 acetate
Cel: Yield; MP; R_f (solvent)	100%[f,g] I.r.: 3384(b): νO–H; 2926(w): νC–H; 1740(s): νC=O lactone; 1228/1030(b): νC–O; ^{13}C n.m.r.: 177.96: C-1 lactone (1 C); 105.51: C-1′ (1 C); 83.15/78.49/78.12/75.88/73.94/73.88/73.33/72.01: C-2/3/4/5/2′/3′/4′/5′ (8 × 1 C); 64.55: C-6 (1 C); 63.16: C-6′ (1 C)	93%[f]0.79 (acetone/MeOH/H_2O 2:1:1) I.r.: 3354(b): νN–H/νO–H; 2924(w): νC–H; 1656(s): νC=O amide I; 1540 (w): δN–H amide II; 1258/1038(b): νC–O; ^{13}C n.m.r.: 172.61: C-1 amide (1 C); 135.21: –CH= allyl (1 C); 115.19: =CH_2 allyl (1 C); 104.06: C-1′ (1 C); 82.59/77.06/76.57/73.98/71.78/71.63/70.88/70.22: C-2/3/4/5/2′/3′/4′/5′ (8 × 1 C); 62.52: C-6 (1 C); 61.36: C-6′ (1 C); 40.79: N–CH_2– allyl (1 C)	28% [h]
Glc_7: Yield; MP; R_f (solvent)	88%; 189°C0.55, tailing(acetone/EtOH/H_2O 2:1:1) [i]	63%; 201°C0.73 (acetone/EtOH/H_2O 2:1:1) I.r.: 3374(b): νO–H; 2930(w): νC–H; 1650(s): νC=O amide I; 1544(w): δN–H amide II; 1154/1026 νC–O; ^{13}C n.m.r.: 174.14: C^{I}-1 amide (1 C); 133.60: –CH= allyl (1 C); 115.67: =CH_2 allyl (1 C); 100.84–99.73: C^{chain}-1; 82.01–71.08: C-2/3/4/5; 69.47: C^{VII}-4 (1 C); 62.25: C^{I}-6 (1 C); 60.58–60.38: C^{chain}-6; 41.31: N–CH_2– allyl (1 C)	49% [h]

[a] Yields in per cent of theoretical amount.
[b] MP, melting points uncorrected.
[c] R_f: solvent and ratio (v/v) given in brackets.
[d] *FT*i.r.: wavenumbers in cm^{-1}.
[e] NMR: 400 MHz (^{1}H); 100 MHz (^{13}C), D_2O (O–Ac compounds: $CDCl_3$), δ in ppm.
[f] MP not measurable owing to hygroscopicity.
[g] R_f not detectable owing to decomposition on silica.
[h] MP, R_f and spectral data identical to those of *Table 8*.
[i] Spectral data identical to those reported previously[4]

2-3861(97)00443-6O-Acetylated 5-OH unprotected *N*-allylaldonamides. A total of 25 mmol of peracetylated aldonolactone is dissolved in 50 ml of dry THF under an inert atmosphere (N_2 or Ar). A total of 30 mmol (2.3 ml) of allylamine is added and the solution is kept under nitrogen for 24 h. Evaporation of the solvent and excess allylamine under reduced pressure provides a pale yellow to brown syrup, which is dissolved in 100 ml ethyl acetate and extracted with 1 M KH_2PO_4 solution, water, saturated $NaHCO_3$ solution, and again three times with water. After drying the organic layer over $MgSO_4$ and concentrating the solution under reduced pressure (to $\leq$ 50 ml) a total of 50 g of silica (40 μm, 480 m2 g^{-1}) is added and the suspension is evaporated to dryness. Chromatography (eluent: toluene/acetone $\approx$ 3:1 v/v, adjusted to $R_f \approx 0.25$) yields the pure aldonamides as colourless compounds.

O-Acetylated *N*-allylaldonamides. To a solution of 11 mmol of the partially acetylated aldonamide in 50 ml of dry THF are added a total of 2.2 ml (23 mmol) of acetic anhydride, 2.3 ml (17 mmol) of triethylamine, and 49 mg (400 μmol) of 4-(*NN*-dimethylamino)pyridine (DMAP). After a reaction time of 30 min a total of 100 ml of ethyl acetate and 100 ml of water is added and stirring is continued for 15 min. The aqueous layer is extracted with ethyl acetate (three times) and the combined organic solutions are extracted five times with water. Drying with $MgSO_4$ and evaporation of the solvent under reduced pressure provides a colourless product, which was pure in most cases according to thin layer chromatography. Otherwise, purification was achieved by chromatography.

Reactions according to path b, Scheme 2

Aldonic acid lactones. The oxidation was carried out according to Frush and Isbell[11] with bromine in aqueous solution buffered by $CaCO_3$, which is best for up-scaling preparations. To a cooled solution (0–5°C) of 30 mmol of the native carbohydrate in 500 ml of water are added a total of 12 g (120 mmol) of $CaCO_3$ and—with exclusion of light—a total of 1.8 ml (36 mmol) of bromine. The reaction mixture is stirred for 12 h in the dark and allowed to warm up to room temperature. After filtration to remove excess $CaCO_3$, the solution is treated with the calculated amount of oxalic acid dihydrate (5.67 g, 45 mmol, dissolved in 30 ml of water) and stirred under cooling with ice/water for 10 min. The precipitated calcium oxalate is filtered off and the solution is funnelled into a suspension of 17 g (60 mmol) of Ag_2CO_3 in 20 ml of water. After further filtration, partial removal of the solvent, and ion exchange chromatography (Amberlite IR-120/H^+, Fluka) the eluate is freed from colloidal silver by filtration through an ultramembrane (3 kDa exclusion size, Filtron, 4–5 bar nitrogen). Removal of the solvent under reduced pressure and lyophilization provides the aldonolactones as very hygroscopic powders.

N-Allylaldonamides. The conversion of the lactone to the amide was achieved as described previously for *N*-allylmaltoheptaonamide[5]. In the case of this carbohydrate, purification by chromatography over DEAE-Sephadex A-25/Cl^- instead of silica was preferred in up-scaled preparations. In the case of other mono- and disaccharides precipitation of the crude product in DMF by isopropanol was not possible. Here, the raw aldonamide was purified chromatographically after evaporation of DMF under a pressure of $<$ 10 mbar.

O-Acetylated *N*-allylaldonamides. Preparation of various aldonamides was carried out as described previously[5] without any change in the procedure.

Glucosamine derivatives

α-Glucosamine pentaacetate from chitin[12]. To a cooled mixture of 1000 ml (11 mol) of acetic anhydride and 130 ml (2.6 mol) of concentrated sulfuric acid is added a total of 200 g ($\approx$ 0.9 mol GlcNAc) of chitin (Fluka). The reaction mixture is stored for 40 h at room temperature and then heated at 55°C for 12 h. The dark solution is poured into a solution of 480 g (5.8 mol) of sodium acetate and 5.2 l of water and stirred for 12 h. The suspension is neutralized with 10 M NaOH and solid Na_2CO_3 and extracted three times with ethyl acetate. Solvent is partially removed from the combined organic solutions before the addition of 200 g of silica (40 μm, 480 m^2 g^{-1}), and the suspension is dried under reduced pressure. The loaded silica is filled into a column and eluted (toluene/acetone 2:1 v/v). The crude α-acetate is recrystallized twice from the same solvent as used for chromatography. Yield: 14.9 g, 38 mmol, 4% theoretical, MP = 131°C, R_f (toluene/acetone 3:2 v/v) = 0.28; R_f (petroleum ether/ethyl acetate 1:5 v/v) = 0.31.

I.r. (cm^{-1}): 3330(b): νN–H; 2952(w): νC–H; 1750(s): νC=O acetate; 1674(s): νC=O amide I; 1526(w): δN–H amide II; 1230/1042(b): νC–O.

^{1}H n.m.r.: (200 MHz; $CDCl_3$; δ/ppm) 6.15(d): α-H-1, $J^{1,2}$ = 3.9 Hz (1 H); 5.56(d): N–H, exchanged by D_2O (1 H); 5.21/4.48/4.24/4.02(m): H-2/3/4/5/6 (6 H); 2.18/2.07/2.04/2.03/1.93(s): $-CH_3$ acetate (each 3 H).

^{13}C n.m.r.: (100 MHz; $CDCl_3$; δ/ppm) 171.18/170.36/169.89/168.90/168.46: C=O acetate (5 $\times$ 1 C); 90.49: α-C-1 (1 C); 70.46: C-5 (1 C); 69.55: C-3 (1 C); 67.64: C-4 (1 C); 61.49 C-6 (1 C); 50.85: C-2 (1 C); 22.66: $-CH_3$ acetamide (1 C); 20.61/20.40/20.28: $-CH_3$ acetate (4 C).

α-Glucosamine pentaacetate from β-glucosamine hydrochloride[13]. To a solution of 2.2 g (17 mmol) of DMAP and 100 ml (720 mmol) triethylamine in 100 ml (1.06 mol) acetic anhydride is added a total of 20 g (92 mmol) of glucosamine hydrochloride (Fluka) at 80°C in portions. The reaction mixture is stirred for 24 h, diluted with 300 ml of ethyl acetate, poured into 500 ml of ice/water and stirred again for 12 h. The aqueous layer is extracted three times with ethyl acetate. The combined organic solutions are washed with water, saturated $NaHCO_3$ solution and again twice with water. Drying with solid $MgSO_4$, evaporation of the solvent under reduced pressure and chromatography provides the α-anomer of glucosamine pentaacetate. Yield: 24 g, 62 mmol, 67% theoretical, identical properties and spectral data to those obtained using the preparation from chitin.

α-2,3,4,6-Tetraacetylglucosamine chloride[13]. To a cooled solution ($-$ 10°C) of 1.6 ml of concentrated hydrochloric acid ($\approx$ 20 mmol HCl) and 38 ml of acetic chloride a total of 10 g (26 mmol) of α-glucosamine acetate is added, and the reaction mixture is stirred for 4 days. After evaporation of all volatile compounds under reduced pressure, a total of 20 ml of methylene chloride is added to the brown residue and the solution is filtered as fast as possible over a 3 cm layer of silica. Evaporation of the solvent and drying *in vacuo* provides the α-chloride of acetylated glucosamine.

Yield: 7.8 g, 21 mmol, 82% theoretical, R_f (petroleum benzine/ethyl acetate 1:5 v/v) = 0.53.

Tetraacetyl-(β-1-O-allyl)glucosamine[14,15]. To a well stirred suspension of 5 g (20 mmol) of $Hg(CN)_2$ in 25 ml of dry nitromethane are added a total of 2 ml (20 mmol) of allyl alcohol and—in 16 portions each over 30 min—a total of 6.4 g (20 mmol) of α-2,3,4,6-tetraacetylglucosamine chloride. The reaction mixture is stirred for 12 h, filtered to remove mercury salts, and dried in a rotary evaporator. Saccharides are extracted from the solid by 100 ml of chloroform. Filtration, drying of the solution with $MgSO_4$ and evaporation of the solvent under reduced pressure provides the crude product, which is purified by chromatography (eluent: ethyl acetate) and recrystallization twice from ethanol. Yield: 1.7 g, 4.4 mmol, 22% theoretical, R_f (ethyl acetate) = 0.42, MP = 160°C.

I.r. (cm^{-1}): 3298(b): νN–H; 3080(w): νH–C=; 2934(s): νC–H; 1750(s): νC=O acetate; 1162(s): νC=O amide I; 1540(w): δN–H amide II; 1374(s): δCH_3; 1236/1046(b): νC–O.

^{13}C n.m.r.: (100 MHz; $CDCl_3$; δ/ppm) 170.71/170.55/170.13/169.27: C=O acetate (4 × 1 C); 133.57: –CH=allyl (1 C); 117.57: $=CH_2$ (1 C); 99.65: β-C-1 (1 C); 72.42/71.76/68.81: C-3/4/5 (3 × 1 C); 69.86: O–CH_2–allyl (1 C); 62.20: C-6 (1 C); 54.68: C-2 (1 C); 23.22: $-CH_3$ acetamide (1 C); 20.65/20.61/20.55: $-CH_3$ acetate (3 × 1 C).

ACKNOWLEDGEMENTS

This work has been supported by the Bundesministerium für Forschung und Technologie der Bundesrepublik Deutschland within the project "Mesoskopische Polymersysteme", contract BMFT NT 2075/9. Additional support from the "Fonds der Chemischen Industrie" is gratefully acknowledged.

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