Synthesis of Carbohydrate-based Chiral Crown Ethers as Ligands in Asymmetric Hydrogenation

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Dedicated to Prof. Dr. Peter Köll on the occasion of his 60th birthday

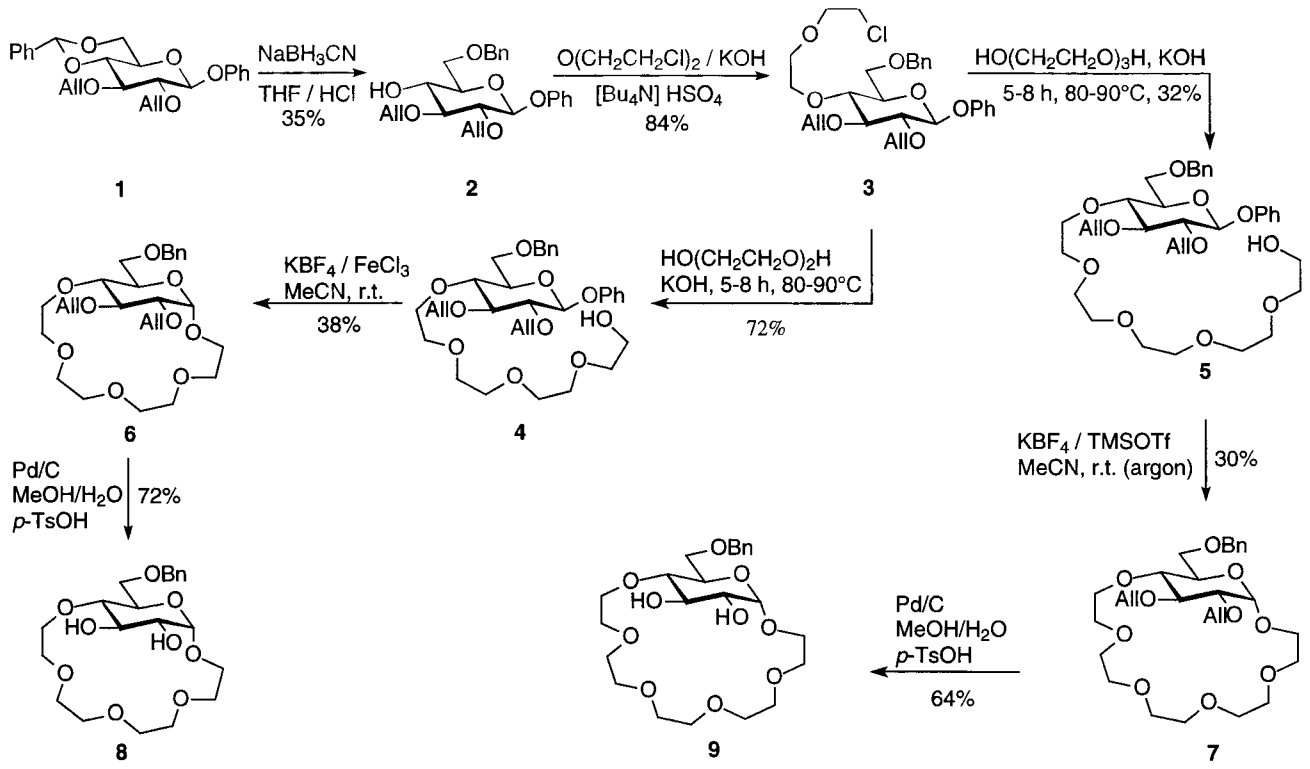
Abstract: Starting from phenyl 2,3-di-*O*-allyl-4,6-*O*-benzylidene-β-D-glucopyranoside (**1**) the chiral crown ethers **6** and **7**, containing a 1,4-bridged α-D-glucopyranoside moiety, were synthesized in four steps via phenyl 2,3-*O*-allyl-6-*O*-benzyl-β-D-glucopyranoside (**2**). To build up the corresponding polyethylene glycol side chain at 4-position, compound **2** was subsequently alkoxylated with bis(2-chloroethyl)ether and diethylene glycol or triethylene glycol yielding via **3** the polyethylene glycol derivatives **4** and **5**, respectively. On a similar way phenyl 2,3-di-*O*-allyl-6-*O*-benzyl-4-*O*-{2-[ω-hydroxypenta(oxyethylene)ethyl]}-β-*D*-galactopyranoside (**15**) was prepared from phenyl 4,6-*O*-benzylidene-β-*D*-galactopyranoside (**10**) via the intermediates **11**, **12** and **13**. The chiral crowns **6**, **7**, and **16** were obtained in yields of 26–38% by intramolecular transglycosylation of **4**, **5**, and **15**, respectively. Whereas a high α-stereoselectivity was found for the cyclization of the 1,4-bridged D-glucose crowns **6** and **7**, galactose derivative **15** gave the β-glycosidic linked crown **16**. In order to obtain the rhodium chelates **18** and **20** as precatalysts for asymmetric hydrogenations, the *gluco*-crown ethers **6** and **7** were deallylated to **8** and **9** and phosphorylated under anaerobic conditions giving the bis(phosphinic esters) **17** and **19**. The latter were used as ligands for **18** and **20**. Finally, asymmetric hydrogenations of amino acid precursors **21a–d** were investigated in the presence of the rhodium chelates **18** and **20**. Under hydrogen, they show as catalysts in different solvents a diminished range of enantioselectivity in comparison with an analogous complex without such a crown ether ring. This can be explained by a stiffening effect of the anellated ring on the chelate ring conformation which is confirmed by the unusually uniform CD-spectra of **20** in solvents of different polarity.

Key words: crown compounds, chiral auxiliaries, homogeneous catalysis, hydrogenations, ligands, rhodium, carbohydrates

Carbohydrate-based chiral crown ethers find increasing interest in asymmetric organic synthesis.[1–10] Therefore, these compounds should be useful tools for the separation of enantiomers, chiral recognition in enzymatic reactions, and for the control of asymmetric syntheses. However, only a few of them proved to be effective in enantioselective reactions.[2b,3b,4,5,7c]

Rhodium(I) chelates of D-hexopyranoside-2,3-*O*-bisphosphinites are extremely useful in the asymmetric hydrogenation of amino acid precursors[11] and have even found application in the industrial production of L-DOPA.[12] Our aim was to synthesize analogous catalysts containing an anellated crown ether-like ring in the 1,4-position of the carbohydrate. Since it is well known that solvent polarity and the formation of cryptate species with alkali ions strongly influence the conformation of crown ethers,[13] we wanted to investigate whether the tuning of these effects would increase the enantioselectivity of these new catalysts. More detailed background information on asymmetric hydrogenation can be found in the latest review by Brown.[14]

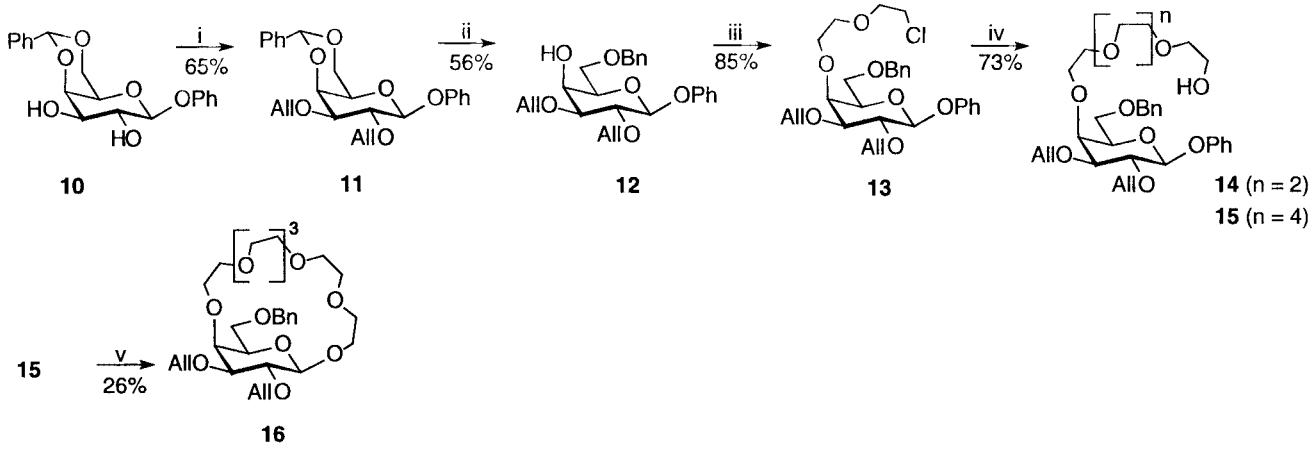
Based on a strategy reported before,[8] the 17-membered and 20-membered macrocyclic compounds **6** and **7**, were synthesized in four steps according to Scheme 1. At first, the benzylidene acetal of phenyl 2,3-di-*O*-allyl-4,6-*O*-benzylidene-β-D-glucopyranoside (**1**) was reductively cleaved using a method by Garegg et al.[15] The major product, phenyl 2,3-di-*O*-allyl-6-*O*-benzyl-β-D-glucopyranoside (**2**),[16] was separated by column chromatography and etherified with bis(2-chloroethyl)ether under phase transfer conditions (catalyst: tetrabutylammonium hydrogen sulfate) giving the diethylene glycol derivative **3** in moderate yield. Compound **3** was the starting material for the synthesis of tetraethylene glycol derivative **4** and pentaethylene glycol derivative **5** by alkoxylation with diethylene glycol and triethylene glycol, respectively, in the presence of potassium hydroxide. This synthetic step requires exact compliance with the given reaction conditions, because HCl-elimination competes more or less efficiently depending on the base and the solvent used. The best yields of **4** (72%) and **5** (32%) were obtained by adding **3** to a solution of KOH in the corresponding glycol (excess) at 80–90 °C under vigorous stirring. Finally, an intramolecular transglucosylation of **4** forming crown ether **6** was carried out in acetonitrile with Fe(III) chloride for the activation of the glycoside and KBF_4 as template reagent. Exclusively the α-anomer (C-1: δ = 97.1; doublet of 1-H: δ = 4.86, $J_{1,2}$ = 3.2 Hz) was formed and isolated in a yield of 38% (Scheme 1). Cyclizations of longer-chain ethylene glycol derivatives were more effective when trimethylsilyl triflate (TMSOTf) was used instead of Fe(III) chloride. Thus, pentaethylene glycol **5** gave in the presence of TMSOTf exclusively the α-anomeric crown **7** (C-1: δ = 97.7; doublet of 1-H: δ = 4.84, $J_{1,2}$ = 3.4 Hz) in 30% yield. Deallylation of the α-D-*gluco*-crowns **6** and **7** was carried out according to literature[17] by heating in aqueous methanolic solution with palladium-on-charcoal and catalytic amounts of *p*-toluenesulfonic acid (Scheme 1).



Scheme 1 Synthesis of the α-glycosidic linked *gluco*-crown ethers

In order to synthesize β-glycosidic linked crown ethers, ethylene glycol substituted D-galactose moieties were synthesized as starting materials (Scheme 2) using the same synthetic strategy as described in Scheme 1 for chiral crowns with D-*gluco*-configuration. Scheme 2 shows the reaction steps starting with phenyl 4,6-*O*-benzylidene-β-D-galactopyranoside (**10**).

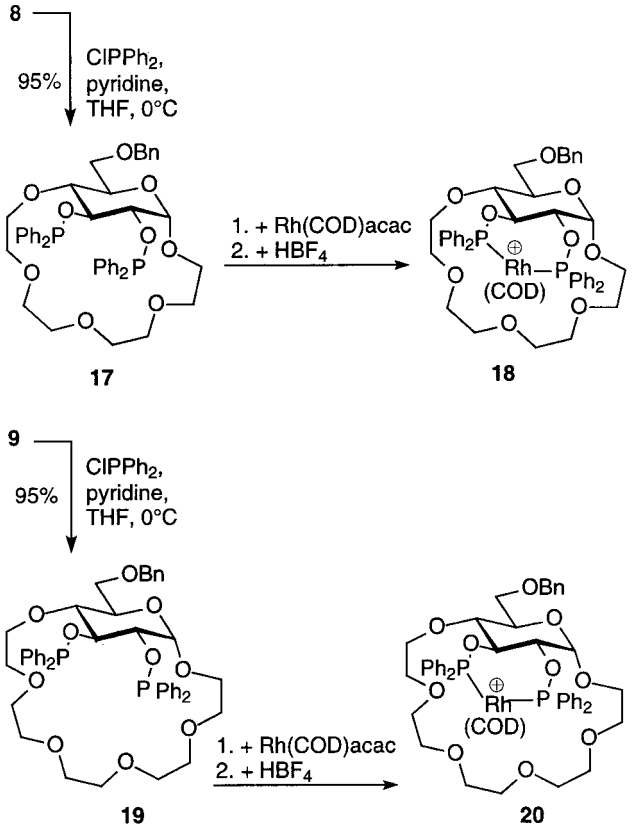
The allylation procedure generating the 2,3-di-*O*-allyl derivative **11** from phenyl 4,6-*O*-benzylidene-β-D-galactopyranoside (**10**)[11] is similar to those reported in the literature.[18,19] The reductive benzylidene acetal opening of **11** to the benzyl derivative **12** required a longer reaction time (48 h) than the benzylidene acetal opening of the glucose derivative **1**. Furthermore, it is accompanied by a relatively unfavourable product ratio of 6-*O*-benzyl regioisomer **12** to phenyl 2,3-di-*O*-allyl-4-*O*-benzyl-β-D-galactopyranoside (about 1:1). However, this mixture could be separated by column chromatography; the pure 6-*O*-benzyl isomer **12** was isolated in 56% yield. Stepwise etherification of **12** via **13** (85%) gave the hexaethylene glycol derivative **15** (73%) in moderate yield (Scheme 2). The intramolecular transacetalation of **15** to **16** was carried out in the presence of TMSOTf. However, a maxi-



Reagents and conditions: i) CH_2=$CHCH_2Br$/NaH/DMF; ii) $NaBH_3CN$/HCl/THF; iii) $O(CH_2CH_2Cl)_2$/50% KOH/THF/PTC; iv) KOH/$HOCH_2(CH_2OCH_2)nCH_2OH$; v) TMSOTf/$Cl(CH_2)_2Cl$/KBF_4/$NaBF_4$

Scheme 2 Synthesis of the β-glycosidic linked *galacto*-crown ethers

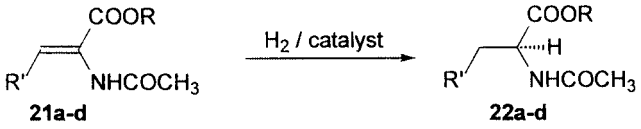
mum yield of 26% was achieved only if the reaction conditions given in the experimental part were exactly kept. At this time the starting material was still not completely converted. As expected, the β-glycosidic bridged macrocycle **16** (C-1: δ = 103.8; doublet of 1-H: δ = 4.23, $J_{1,2}$ = 7.3 Hz) was formed due to the orientation of the glycol chain at the 4-position which allows only a β-attack. In contrast to the long-chain ethylidene glycol galactoside **15**, cyclisation of phenyl 2,3-di-*O*-allyl-6-*O*-benzyl-4-*O*-{2-[ω-hydroxytri(oxyethylene)ethyl]}-β-D-galactopyranoside (**14**) was not successful. The shorter ethylene glycol chain is not long enough to close a ring free of tension.



Scheme 3 Synthesis of the chelates **18** and **20** (precatalysts for hydrogenations)

The α-D-*gluco*-crown ethers **8** and **9** gave in reaction with chloro-diphenylphosphine the non-crystalline bis(phosphinic ester) **17** and the crystalline bis(phosphinic ester) **19** in yields of 95%. The NMR spectra of the non-crystalline product **17** showed impurities. Because bis(phosphinic esters) are very sensitive to oxidation and hydrolysis, chelate **18** was directly generated from this product **17** by treatment with Rh(COD)acac/HBF_4 (Scheme 3). Upon reaction with Rh(COD)acac/HBF_4 the 20-membered ligand **19** isolated as a pure solid gave the chelate **20** in much better quality.

The chelates **18** and **20** were used as precatalysts for the hydrogenation of the 2-*N*-acyl-2-dehydroamino acid derivatives **21a–d** (Scheme 4). The microanalysis of compound **18** deviated from the theoretical values. ^{31}P NMR analysis and mass spectrum confirmed that the desired target chelate is the major component contaminated by a complex of one monophosphinite of **8**. Because purification of such chelates by recrystallization were not successful, this crude product was used for preliminary hydrogenation experiments (Table 1). The complex was highly active and the selectivity outcome comparable with the results of the hydrogenations using the pure chelate **20** (Table 2). This indicates, that the desired complex **18** should be the main catalytic active component in the mixture and that the influence of the impurities seems to be negligible.



a: R = H, R' = H; **b**: R = Me, R' = H; **c**: R = H, R' = Ph; **d**: R = Me, R' = Ph

Scheme 4 Hydrogenation of the 2-*N*-acyl-2-dehydroamino acid derivatives **21a–d**

The aim of these hydrogenation experiments was to examine whether catalysts modified by an anellated crown ether ring change their enantioselectivity under the influence of alkali ions. Earlier, we found that the enantioselectivity of rhodium(I) chelates – particularly of the methyl 4,6-*O*-benzylidene-2,3-*O*-bis(diphenylphosphino)-α-D-glucopyranoside (Me-α-glup) – in asymmetric hydrogenations of 2-*N*-acyldehydroamino acid esters showed a considerable solvent dependence, which in the extreme case of benzene as solvent even led to a change

Table 1 Hydrogenation of 2-*N*-Acyl-2-dehydroamino Acid Derivatives Using Precatalyst **18**[a]

Substrate	R	R'	MeOH		C_6H_6		H_2O	
			t/2 min	% ee (*S*)-**22**	t/2 min	% ee (*S*)-**22**	t/2 min	% ee (*S*)-**22**
21a	H	H	1	59	400	48	455	14
21b	Me	H	1	75 (73)	1	41 (4 *R*)	73	34 (22)
21c	H	Ph	5	55 (72)	41	58 (70 *S*)		
21d	Me	Ph	5	57 (72)	3	43 (6 *R*)		

[a] Reference values published for [Rh(Me-α-glup)(COD)]BF_4 (**23**)[11,31] are given in parenthesis. Conditions for hydrogenation: 1 mmol substrate, 0.01 mmol precatalyst **18**, 15 mL solvent, 25 °C, 0.1 MPa.

of the preferred product enantiomer.[11,20] We attribute this large range of enantioselectivity to the changes in the conformation of the seven-membered chelates, which may result in a nearly enantiomorphic arrangement of the *P*-aryl groups in the intermediate catalyst-substrate complexes. According to a hypothesis of Knowles,[21] modified by Seebach,[22] the spatial orientation of such *P*-aryl groups determines the enantioselectivity and we succeeded in calculating for some catalysts the energy barriers for the preferred conformations.[23] Some of them which show approximately enantiomorphic aryl orientation are found by NMR in solution or estimated by X-ray structure analysis. It is well known that crown ethers suffer considerable conformational change under the influence of different solvents[13] or by complexation of alkali ions. Consequently, it seemed reasonable to look for similar effects on catalysts with ligands analogous to Me-α-glup carrying an anellated crown ether ring and to expect an influence on the enantioselectivities as consequence.

The results indicate a reduced solvent influence on the new complex **18** compared to the parent complex [Rh(Me-α-glup)(COD)]BF_4 (**23**) (Table 1). Particularly, the absence of the selectivity inversion for the esters **21b** and **21d** going from methanol to benzene as solvent shall be mentioned here. Furthermore, we noted that the addition of alkali ions has no influence on the enantioselectivity. For the hydrogenation of ester **21b** in the presence of 0.1 mmol Li-, Na-, K-, Rb- or Cs-tetrafluoroborate the deviation from the control remained below Δ% ee = 3 in all three solvents. The same is valid for the hydrogenation of acid **21a** in methanol. These results indicate that anellation with the crown ether ring may cause a restriction of the conformational lability of the seven-membered chelate ring, thus limiting the range of enantioselectivity.

The distinctly higher enantioselectivity for the ester **21b** compared to the corresponding acid **21a** and the ester **21d** is surprising. The low solubility of the substrate **21a** in benzene and water causes the time for half hydrogenation (t/2) in these solvents to be very large.

Precatalyst **20**, with one additional oxyethylene unit, shows nearly the same gradation in dependence of the applied substrates and solvents and in most cases somewhat lower enantioselectivities than precatalyst **18** (Table 2). Significantly higher enantiomeric excesses were found only in benzene with the substrate acids **21a** and **21c** (71 and 80% ee).

The hydrogenations in water were completed by measurements in the presence of Triton® X100 as a solubility promoter. The well known promoting effect of such amphiphiles on the activity and enantioselectivity[11,24–26] also occurred with the catalyst released from **20** (44→69% ee, Table 3). Again we could not find a distinct effect of alkali ions on the selectivity. Only in benzene as the solvent the hydrogenation of acetamidocinnamic acid (**21c**) was influenced by lithium tetrafluoroborate (80→64% *ee*). We assume that this effect is not caused by the formation of a lithium cryptate, deviating the conformation of the catalyst, but mainly by generation of ion pairs between lithium and the substrate acid which thereby changes the type of substrate coordination to the catalyst. This could explain the absence of this effect both in polar solvents and with the substrate ester **21d** in benzene. Such ion pair formation in benzene should be prevented for the other, less soluble alkali salts.

From these results we conclude that for the catalysts generated from **18** as well as from **20** the conformation of the seven-membered chelate ring is stiffened by the crown ether-like anellation. The enantioselectivity remains relatively constant under varying conditions in contrast to the behaviour of the original parent precatalyst [Rh(Me-α-glup)(COD)]BF_4 (**23**).[27] A conformational change resulting in a more or less enantiomorphic orientation of the *P*-aryl groups seems to be not noticable for the precatalyst **20** because its CD-spectra are similar in methanol and benzene (Figure). The reverse is the case for the precatalyst **23** which in benzene hydrogenates the substrate esters as **21b** and **21d** under increase of the unexpected (*R*)-enantiomer part and which CD-spectra in both solvents show nearly enantiomorphic shape of its curves (Figure).

CD spectra can only hint at tendencies for conformational change in different solvents. It is important to state that it is not possible to predict the direction of enantioselectivity from the CD spectra of precatalysts because this depends from the preequilibria between diastereomeric (*Re*)- and (*Si*)-catalyst-substrate complexes as well as their different hydrogenation kinetics,[28–30] and is strongly influenced by the nature of the substrate.

Table 2 Hydrogenation of 2-*N*-Acyl-2-dehydroamino Acid Derivatives Using Precatalyst **20** (For Conditions of Hydrogenation, see Table 1)

Substrate	R	R'	MeOH		C_6H_6		H_2O		H_2O + Triton® (0.1 mmol)[a]		H_2O + Triton® (0.5 mmol)[a]	
			t/2 min	% ee (*S*)-**22**	t/2 min	% ee (*S*)-**22**	t/2 min	% ee (*S*)-**22**	t/2 min	% ee (*S*)-**22**	t/2 min	% ee (*S*)-**22**
21a	H	H	1	56	485	71			6	42	3	42
21b	Me	H	1	71	1	36	20	44	4	69	3	70
21c	H	Ph	3	52	31	80						
21d	Me	Ph	3	53	2	41						

[a] Triton® X100, amphiphile as solubility promoter.

Table 3 Hydrogenation with Precatalyst **20** in the Presence of Alkali Salts (For Conditions of Hydrogenation, see Table 1)

Alkali Salt (MBF_4)	**21b** H_2O		**21b** H_2O + Triton® (0.1 mmol)		**21d** C_6H_6		**21c** C_6H_6	
M	t/2 min	% ee (*S*)-**22b**	t/2 min	% ee (*S*)-**22b**	t/2 min	% ee (*S*)-**22d**	t/2 min	% ee (*S*)-**22c**
–	20	44	4	69	2	41	31	80
Li	31	43	7	68	2	45	30	64
Na	33	40	6	68	1	41	18	83
K	32	42	6	68	1	41	27	82
Rb	37	42	9	68	2	41	20	82
Cs	37	41	8	68	2	41	28	83

[a] In the presence of 0.1 mmol MBF_4 in 15 mL of the reaction mixture.

Column chromatography: Silica gel 60 (63−200 µm, Merck); TLC: Silica gel foils 60 F_{254} (Merck). NMR spectra: Bruker AC 250 and ARX 400 equipment, ^{1}H NMR and ^{13}C{^{1}H} NMR referenced to TMS, IR spectra: Nicolet FTIR Protegé 460 (pellets, KBr). Melting points: Polarizing microscope Leitz (Laborlux 12 Pol) equipped with a hot stage (Mettler FP 90). The hydrogenations and gaschromatography of the products were conducted as described in reference 11. Acidic hydrogenation products were esterified before GC analysis. Chemicals: Pd/charcoal (Fluka), chlorodiphenylphosphine (Fluka), [Rh(COD)(acac)].[31] CD spectra: Jasco J710. Measurements were performed in anhydrous and degassed solvents at a concentration of $2\cdot10^{-4}$ molL^{-1} and a cell length of 1 cm. The solutions were handled under argon and the cuvettes were equipped so as to exclude air and moisture during filling and measurement.

Phenyl 2,3-Di-*O*-allyl-6-*O*-benzyl-β-D-glucopyranoside (2)

To a stirred solution of **1**[19] (5.0 g, 13.8 mmol) in anhyd THF (85 mL) were added $NaBH_3CN$ (4.40 g, 70.0 mmol), solid Methylorange (100 mg) and activated molecular sieve 3Å (2.0 g). After cooling the mixture to 0 °C, Et_2O (freshly saturated with HCl) was added dropwise taking care that the temperature did not exceed 10 °C. HCl addition was stopped when the solution took on a pink colour, and the mixture was stirred at r.t. for 16 h (TLC control) and was followed by addition of H_2O (150 mL) and repeated extractions with Et_2O (total 150 mL). Subsequently, the combined organic layers were neutralized with sat. aq $NaHCO_3$ solution (20 mL), washed with H_2O (20 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue, a mixture of **2** and phenyl 2,3-di-*O*-allyl-4-*O*-benzyl-β-D-glucopyranoside was purified by column chromatography; R_f 0.46 (toluene/EtOAc, 5:1 v/v) (Table 4).

Anal. calcd for $C_{26}H_{32}O_6$ (440.5): C, 70.89; H, 7.32. Found: C, 70.86; H, 7.53.

Phenyl 2,3-Di-*O*-allyl-4-[2-(2-chloroethoxy)ethyl]-6-*O*-benzyl-β-D-glucopyranoside (3)

A vigorously stirred solution of **2** (8.38 g, 19.5 mmol) in THF (24 ml) was added dropwise to a mixture of 50% aq KOH (40 mL), bis(2-chloroethyl)ether (40 mL, 0.34 mol) and catalytic amounts of tetrabutylammonium hydrogen sulfate. The mixture was stirred for 4−5 h at 50 °C (TLC control) and then allowed to stand overnight at r.t. After neutralization with 50% aq AcOH and addition of H_2O (50 mL), the product was extracted with $CHCl_3$ (3 × 100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by column chromatography (Table 4).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54−7.24 (m, 10 H, 2 C_6H_5), 6.26−6.13 (m, 2 H, 2 CH_2CH=CH_2), 5.55−5.38 (m, 4 H, 2 CH_2CH=CH_2), 5.1 (d, 1 H, $J_{1,2}$ = 7.6 Hz, 1-H), 4.84, 4.77 (2 d, 2 H, J = 12.1 Hz, PhCH_2), 4.7−4.49 (m, 4 H, 2 CH_2CH=CH_2), 4.19 (ddd, 1 H, $J_{4,5}$ = 10.5, $J_{5,6}$ = 5.3, $J_{5,6'}$ = 3.7 Hz, 5-H), 4.07−3.63 (m, 13 H, 2-H, 3-H, 4-H, 6-H, 6'-H, 4 CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.7, 135.4 (2 CH_2CH=CH_2), 138.7−117.5 (2 C_6H_5), 117.4, 117.2 (2 CH_2CH=CH_2), 102.0 (C-1), 84.4 (C-2), 81.9, 78.6, 75.5, 74.9 (C-3, C-4, C-5), 74.9, 74.2, 73.8, 72.5, 71.6, 71.2, 69.2 (C-6, 6 CH_2), 43.1 (CH_2Cl).

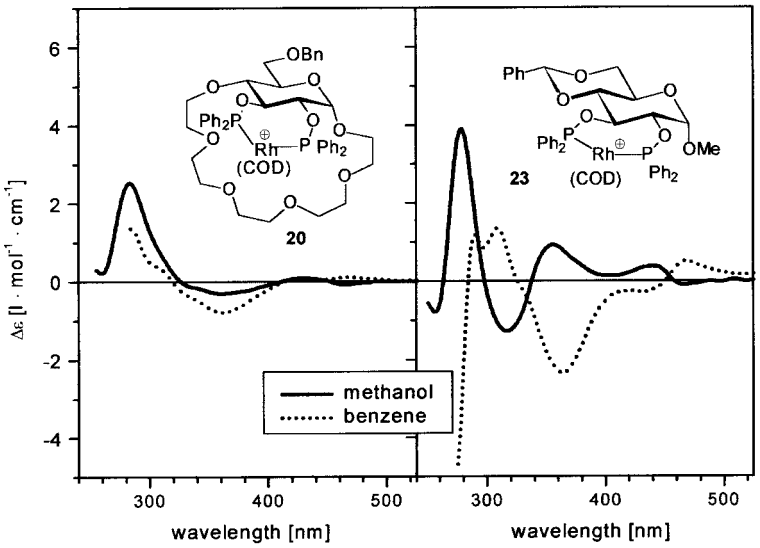


Figure CD-spectra of the precatalysts **20** and **23** in methanol or benzene ($c = 2\cdot10^{-4}$ molL^{-1}).

Table 4 Data of the *gluco*-Precursors **2–5**, *galacto*-Precursors **11–15**, *gluco*-Crowns **6–9**, *galacto*-crown **16**, *gluco*-Precatalysts **18**, **20**

Product	Precursor	Yield (%)	Mp (°C) (solvent)	Formula (molar mass)	$[\alpha]_D^{24}$ $CHCl_3$ (*c*)	R_f (eluents v/v)
2	**1**	75	colorless syrup	$C_{26}H_{32}O_6$ (440.5)	–[a]	0.46 (toluene/ EtOAc, 5:1)
3	**2**	84	colorless syrup	$C_{29}H_{37}ClO_7$ (533.1)	–15.0 (1.45)	0.28 (toluene/ EtOAc, 5:1)
4	**3**	72	colorless syrup	$C_{33}H_{46}O_{10}$ (602.7)	–[a]	0.30 (CH_2Cl_2/MeOH, 50:1)
5	**3**	32	brownish syrup	$C_{35}H_{50}O_{11}$ (646.8)	−21.4 (1.3)	0.48 (EtOAc/acetone, 5:1)
6	**4**	38	colorless syrup	$C_{27}H_{40}O_9$ (508.6)	–[a]	0.40 (hexane/EtOAc, 1:2)
7	**5**	37	colorless syrup	$C_{29}H_{44}O_{10}$ (552.7)	+63.8.0 (1.5)	0.27 (toluene/EtOAc/MeOH, 7.5:1:0.5)
8	**6**	72	colorless syrup	$C_{21}H_{32}O_9$ (428.5)	–[a]	0.24 ($CHCl_3$/MeOH, 10:1)
9	**7**	64	colorless syrup	$C_{23}H_{36}O_{10}.H_2O$ (490.6)	+68.3 (1.36)	0.34 ($CHCl_3$/MeOH, 10:1)
11	**10**	65	175 (EtOH)	$C_{25}H_{28}O_6$ (424.4)	−13.4 (1.04)	
12	**11**	56	114−115	$C_{25}H_{30}O_6$ (426.4)	−14.7 (1.02)	0.14 (toluene/ EtOAc, 15:1)
13	**12**	85	55−57	$C_{29}H_{37}O_7$ (533.0)	−18.2 (1.00)	0.29 (heptane/EtOAc, 3.5:1)
14	**13**	73	colorless syrup	$C_{33}H_{46}O_{10}$ (602.5)	−13.4 (1.03)	0.23 (EtOAc)
15	**13**	73	colorless syrup	$C_{37}H_{54}O_{12}$ (690.8)	−16.6 (0.99)	0.40 (EtOAc/acetone, 5:1)
16	**15**	26	colorless syrup	$C_{31}H_{48}O_{11}$ (596.7)	−11.9 (0.37)	0.14 (EtOAc)
18	**8**	90	crystalline [b]	$C_{53}H_{62}BF_4O_9P_2Rh$ (1094.7)[c]		
20	**19**	99	crystalline [b]	$C_{55}H_{66}BF_4O_{10}P_2Rh$ (1138.8)[d]		

[a] $[\alpha]_D$ was not determined.
[b] Mp was not determined because of the high sensitiveness of the compound.
[c] MS-FAB pos., matrix NBA $[M - BF_4]^+$ 1007; $[M - BF_4 - COD]^+$ 899; impurity 823; 715.
[d] MS-FAB pos., matrix NBA $[M - BF_4]^+$ 1051; $[M - BF_4 - COD]^+$ 943.

Anal. Calcd for $C_{29}H_{37}ClO_7$ (533.1): C, 65.34; H, 7.00; Cl, 6.65. Found: C, 65.10; H, 7.24; Cl, 7.00.

Phenyl 2,3-Di-*O*-allyl-6-*O*-benzyl-4-*O*-{2[ω-hydroxytri(oxyethylene)ethyl]}-β-D-glucopyranoside (4)

Powdered KOH (6.0 g, 106.9 mmol) was dissolved in diethylene glycol (20 mL) under stirring and moderate heating. The solution was poured onto **3** (2.8 g, 5.2 mmol) under vigorous stirring and heated for about 5 h at 80−90 °C. After complete conversion (TLC control), the mixture was diluted with H_2O (30 mL), neutralized with dil aq HCl, and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were dried (Na_2SO_4), concentrated under reduced pressure and compound **4** was separated from the residue by column chromatography (Table 4).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55−7.24 (m, 10 H, 2 C_6H_5), 6.27−6.13 (m, 2 H, 2 CH_2CH=CH_2), 5.55-5.38 (m, 4 H, 2 CH_2CH=CH_2), 5.11 (d, 1 H, $J_{1,2}$ = 7.6 Hz, 1-H), 4.84, 4.77 (2 d, 2 H, J = 11.9 Hz, PhCH_2), 4.7−4.49 (m, 4 H, 2 CH_2CH=CH_2), 4.19 (ddd, 1 H, $J_{4,5}$ = 10.8, $J_{5,6}$ = 5.4, $J_{5,6'}$ = 3.9 Hz, 5-H), 4.07−3.62 (m, 21 H, 2-H, 3-H, 4-H, 6-H, 6'-H, 8 CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.7−117.4 (2 C_6H_5), 135.7, 135.4 (2 CH_2CH=CH_2), 117.3, 117.2 (2 CH_2CH=CH_2), 101.9 (C-1), 84.4 (C-2), 81.8, 78.7, 75.4 (C-3, C-4, C-5), 74.9, 74.1, 73.8, 72.9, 72.5, 71.2, 71.1, 71.0, 70.9, 70.7, 69.3, 62.1 (C-6, 11 CH_2).

Anal. Calcd for $C_{33}H_{46}O_{10}$ (602.7): C, 65.76; H, 7.69. Found: C, 65.30; H, 7.80.

Phenyl 2,3-Di-*O*-allyl-6-*O*-benzyl-4-*O*-{2[ω-hydroxytetra(oxyethylene)ethyl]}-β-D-glucopyranoside (5)

The 2-chloroethoxyethyl derivative **3** (9.62 g, 18 mmol) was treated with a solution of KOH (28.0 g, 0.5 mol) in triethylene glycol (96 mL) and the mixture was worked up (R_f 0,48, EtOAc/acetone, 5:1 v/v) as described for compound **4**. The pure product **5** was isolated as brownish syrup (Table 4).

IR (KBr): ν = 886 cm^{-1} ($\delta_{C\text{-Haxial}}$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33−7.23 (m, 5 H, C_6H_5), 5.99−5.83 (m, 2 H, 2 CH_2CH=CH_2), 5.28−5.09 (m, 4 H, 2 CH_2CH=CH_2), 4.74 (d, 1 H, $J_{1,2}$ = 3.4 Hz, 1-H), 4.61, 4.51 (2 d, 2 H, J = 12.1 Hz, PhCH_2), 4.35−4.08 (m, 4 H, 2 CH_2CH=CH_2), 3.9 (ddd, 1 H, $J_{4,5}$ = 10.6, $J_{5,6}$ = 3.8, $J_{5,6'}$ = 5.5 Hz, 5-H), 3.74−3.34 (m, 25 H, 2-H, 3-H, 4-H, 6-H, 6'-H, 10 CH_2), 3.36 (s, 3 H, OCH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.9, 135.3 (2 CH_2CH=CH_2), 128.7, 128.2, 128.0 (C_6H_5), 117.6, 116.5 (2 CH_2CH=CH_2), 98.2 (C-1), 81.2 (C-2), 79.4, 78.2 (C-3, C-4), 77.8-70.8 (12 CH_2), 70.7 (C-5), 70.4 (C-6), 62.1 (CH_2OH), 55.4 (OCH_3).

Anal. Calcd for $C_{35}H_{50}O_{11}$ (646.8): C, 65.00; H, 7.79. Found: C, 65.46; H, 7.96.

2,3-Di-*O*-allyl-6-*O*-benzyl-1,4-*O*-(3,6,9-trioxaundecan-1,11-diyl)-α-D-glucopyranose (6)

To a stirred solution of **4** (3.33 g, 5.5 mmol), KBF_4 (1.33 g, 10.6 mmol) in anhyd MeCN (130 mL) was added $FeCl_3$ (1.05 g, 6.47 mmol) at r.t. After stirring for 6−8 h the conversion was complete

(TLC control). H_2O (50 mL) was added, the mixture was extracted with $CHCl_3$ (3 × 50 mL), and the dried organic phases (Na_2SO_4) were concentrated under reduced pressure giving a syrupy residue. Pure crown ether **6** was isolated by column chromatography (Table 4).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38−7.23 (m, 5 H, C_6H_5), 6.03−5.86 (m, 2 H, 2 CH_2CH=CH_2), 5.31−5.11 (m, 4 H, 2 CH_2CH=CH_2), 4.86 (d, 1 H, $J_{1,2}$ = 3.2 Hz, 1-H), 4.66, 4.52 (2 d, 2 H, J = 12.1 Hz, PhCH_2), 4.38−3.44 (m, 25 H, 3-H, 4-H, 5-H, 6-H, 6'-H, 10 CH_2), 3.4 (dd, 1 H, $J_{2,3}$ = 9.6 Hz, 2-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.7−127.8 (C_6H_5), 136.2, 135.5 (2 CH_2CH=CH_2), 118.0, 116.5 (2 CH_2CH=CH_2), 97.1 (C-1), 81.0 (C-2), 79.6, 77.6 (C-3, C-4), 74.6, 73.5, 73.1, 72.2, 71.2, 71.1, 71.0, 71.0, 70.9, 69.9, 69.3, 66.8 (C-6, 11 CH_2), 69.7 (C-5).

Anal. Calcd for $C_{27}H_{40}O_9$ (508.6): C, 63.76; H, 7.93. Found: C, 63.93; H, 7.84.

2,3-Di-*O*-allyl-6-*O*-benzyl-1,4-*O*-(3,6,9,12-tetraoxatetradecan-1,14-diyl)-α-D-glucopyranose (7)

To a stirred solution of **5** (0.74 g, 1.45 mmol), KBF_4 (0.37 g, 2.94 mmol) in anhyd MeCN (40 mL) was added TMSOTf (0.39 ml, 2.2 mmol) under cooling (argon atmosphere). Stirring was continued at r.t. up to the conversion was complete (TLC control). Satd aq $NaHCO_3$ solution (20 mL) was added and the mixture was extracted with Et_2O (3 × 40 mL). The dried organic phases (Na_2SO_4) were concentrated under reduced pressure to give a syrupy residue. Pure crown ether **7** was isolated as colourless syrup by column chromatography (Table 4).

IR (KBr): ν = 849 cm^{-1} ($\delta_{C-Hequatorial}$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37−7.23 (m, 5 H, C_6H_5), 6.02−5.84 (m, 2 H, 2 CH_2CH=CH_2), 5.3−5.1 (m, 4 H, 2 CH_2CH=CH_2), 4.84 (d, 1 H, $J_{1,2}$ = 3.4 Hz, 1-H), 4.67, 4.53 (2 d, 2 H, J = 12.1 Hz, PhCH_2), 4.37−3.37 (m, 30 H, 2-H, 3-H, 4-H, 5-H, 6-H, 6'-H, 12 CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.0, 135.4 (2 CH_2CH=CH_2), 128.6, 128.3, 127.8 (C_6H_5), 118.0, 116.7 (2 CH_2CH=CH_2), 97.7 (C-1), 82.0 (C-2), 79.7, 78.2 (C-3, C-4), 74.6-68.8 (13 CH_2), 70.2 (C-5), 67.9 (C-6).

MS (70 eV): *m*/*z* = 511 (M − All).

Anal. Calcd for $C_{29}H_{44}O_{10}$ (552.7): C, 63.03; H, 8.02. Found: C, 62.82; H, 8.11.

6-*O*-Benzyl-1,4-*O*-(3,6,9-trioxaundecan-1,11-diyl)-α-D-glucopyranose (8)

A vigorously stirred suspension of **6** (1.19 g, 2.3 mmol), *p*-toluenesulfonic acid (0.3 g) and Pd/C (0.59 g) in MeOH/H_2O (160 mL, 5:1 v/v) was refluxed for 2−3 h (argon atmosphere, TLC control) and then allowed to cool to r.t. After addition of Et_3N (1 mL), the mixture was filtered (kieselguhr) and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (Table 4).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37−7.24 (m, 5 H, C_6H_5), 4.93 (d, 1 H, $J_{1,2}$ = 3.2 Hz, 1-H), 4.66, 4.53 (2 d, 2 H, J = 12.2 Hz, PhCH_2), 4.17−3.45 (m, 22 H, 2-H, 3-H, 4-H, 5-H, 6-H, 6'-H, 8 CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.8, 128,6, 128.2, 127.9 (C_6H_5), 98.8 (C-1), 78.3 (C-2), 74.0, 73.3 (C-3, C-4), 70.7 (C-5), 73.6, 72.0, 71.5, 71.1, 71.0, 70.8, 70.8, 69.6, 69.4, 67.4 (C-6, 9 CH_2).

Anal. Calcd for $C_{21}H_{32}O_9$ (428.5): C, 58.87; H, 7.53. Found: C, 58.38; H, 7.57.

6-*O*-Benzyl-1,4-*O*-(3,6,9,12-tetraoxatetradecan-1,14-diyl)-α-D-glucopyranose (9)

A vigorously stirred suspension of **7** (1.77 g, 3.2 mmol), *p*-toluenesulfonic acid (0.81 g) and Pd/C (0.80 g) in MeOH/H_2O (160 mL, 5:1 v/v) was refluxed for 2−3 h (argon atmosphere, TLC control) and then allowed to cool on r.t. After the addition of aq satd $NaHCO_3$ solution (2–3 mL), the mixture was filtered (kieselguhr) and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (Table 4).

Anal. Calcd for $C_{23}H_{36}O_{10}.H_2O$ (490.6): C, 56.32; H, 7.81. Found: C, 56.38; H, 7.79.

Phenyl 2,3-Di-*O*-allyl-4,6-*O*-benzylidene-β-D-galactopyranoside (11)

To a stirred solution of **10**[11] (5.0 g, 14.5 mmol) in anhyd DMF (57 mL) was added NaH (4.05 g, 102 mmol) in portions under cooling. Then, allyl bromide (3.7 mL, 43.5 mmol) was added dropwise to the solution at 0 °C while stirring, the mixture was allowed to warm up to r.t. and to react for about 20 h (TLC control). Subsequently, the excess of NaH was carefully decomposed (stirring, cooling) with MeOH/H_2O (40 mL, 1:1 v/v), the mixture diluted with H_2O (100 mL) and the product **11** was extracted with $CHCl_3$ (2 × 50 mL). The combined organic phases were washed with aq $NaHCO_3$ solution (2 × 70 mL) and H_2O (2 × 70 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crystalline product **11** was recrystallized from EtOH (Table 4).

^{1}H NMR (250 MHz,$CDCl_3$): δ = 7.57−6.97 (m, 10 H, C_6H_5), 6.03−5.86 (m, 2 H, 2 CH_2CH=CH_2), 5.55 (s, 1 H, acetal-H), 5.37−5.08 (m, 4 H, 2 CH_2CH=CH_2), 4.94 (d, 1 H, $J_{1,2}$ = 7.8 Hz, 1-H), 4.47−4.20 (m, 6 H, 2 CH_2CH=CH_2, 4-H, 6'-H), 4.07 (dd, 1 H, $J_{6,5}$ = 1.8, $J_{6,6'}$ = 12.4 Hz, 6-H), 3.93 (dd, 1 H, $J_{2,3}$ = 9.6 Hz, 2-H), 3.54 (dd, 1 H, $J_{3,4}$ = 3.5 Hz, 3-H), 3.48 (m, 1 H, 5-H).

^{13}C NMR (62 MHz, $CDCl_3$): δ = 157.6, 137.7, 129.3, 128.9, 128.1, 126.5, 122.6, 117.3 (C_6H_5), 135.1, 135.0 (2 CH_2CH=CH_2), 117.4, 116.7 (2 CH_2CH=CH_2), 102.0, 101.7 (acetal-C, C-1), 78.7, 77.6, 74.1 (C-2, C-3, C-4), 74.0, 71.6, 69.1 (2 CH_2CH=CH_2, C-6), 66.5 (C-5).

Anal. Calcd for $C_{25}H_{28}O_6$ (424.4): C, 70.72; H, 6.65. Found: C, 70.75; H, 6.62.

Phenyl 2,3-Di-*O*-allyl-6-*O*-benzyl-β-D-galactopyranoside (12)

A solution of benzylidene acetal **11** (1.0 g, 2.34 mmol) in anhyd THF (18 mL) was treated with $NaBH_3CN$ (0.884 g, 14.1 mmol) and solid methylorange as described for compound **2**. However, the reaction was only complete after 3−4 d (TLC control). The reaction mixture was worked up as described for **2** and the product purified by column chromatography; colourless crystals (Table 4).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.38−6.99 (m, 10 H, C_6H_5), 6.05−5.87 (m, 2 H, 2 CH_2CH=CH_2), 5.38−5.13 (m, 4 H, 2 CH_2CH=CH_2), 4.90 (d, 1 H, $J_{1,2}$ = 7.9 Hz, 1-H), 4.61, 4.55 (2 d, 2 H, J = 13.1 Hz, PhCH_2), 4.49−4.20 (m, 4 H, 2 CH_2CH=CH_2), 4.06 (dd, 1 H, $J_{4,5}$ = 0.6, $J_{3,4}$ = 3.4 Hz, 4-H), 3.88−3.68 (m, 4 H, 2-H, 5-H, 6-H, 6`-H), 3.46 (dd, 1 H, $J_{2,3}$ = 9.4 Hz, 3-H), 2.35 (br, 1 H, OH).

^{13}C NMR (62 MHz, $CDCl_3$): δ = 157.4, 137.9, 129.3, 128.4, 127.7, 122.5 (C_6H_5), 135.0, 134.5 (2 CH_2CH=CH_2), 117.4, 117.0 (2 CH_2CH=CH_2), 101.7 (C-1), 80.2 (C-2), 78.1 (C-3), 73.9, 73.7 (2 CH_2), 73.6, 66.9 (C-4, C-5), 71.6 (CH_2Ph), 69.2 (C-6).

Anal. Calcd for $C_{25}H_{30}O_6$ (426.4): C, 70.40; H, 7.09. Found: C, 70.46; H, 6.97.

Phenyl 2,3-Di-*O*-allyl-6-*O*-benzyl-4-*O*-[(2-chloroethoxy)ethyl]-β-D-galactopyranoside (13)

To a vigorously stirred solution of **12** (426 mg, 1.0 mmol) in THF (1 mL) was dropwise added a mixture of 50% aq KOH (2 mL),

bis(2-chloroethyl)ether (2 mL) and tetrabutylammonium hydrogen sulfate (20 mg) at r.t. The reaction was complete after about 4-5 days (TLC control). After neutralisation with 10% aq AcOH, the product was extracted with $CHCl_3$ (3 × 10 mL). The combined organic phases were dried (Na_2SO_4) and concentrated under reduced pressure in a rotary evaporator. The residue was purified by column chromatography (Table 4).[32]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.4−6.98 (m, 10 H, C_6H_5), 6.06−5.88 (m, 2 H, 2 CH_2CH=CH_2), 5.39−5.12 (m, 4 H, 2 CH_2CH=CH_2), 4.88 (d, 1 H, $J_{1,2}$ = 7.9 Hz, 1-H), 4.57, 4.53 (2 d, 2 H, J = 11.9 Hz, CH_2Ph), 4.49−4.22 (m, 4 H, 2 CH_2CH=CH_2), 4.08 (m, 1 H, 5-H), 3.89−3.57 (m, 12 H, 2-H, 4-H, 6-H, 6'-H, 4 CH_2), 3.43 (dd, 1 H, $J_{3,4}$ = 3.1, $J_{2,3}$ = 9.7 Hz, 3-H).

^{13}C NMR (62 MHz, $CDCl_3$): δ = 157.5, 138.8, 129.3, 128.4, 127.8, 127.7, 122.4 (C_6H_5), 135.4, 134.9 (2 CH_2CH=CH_2), 116.7, 116.6 (2 CH_2CH=CH_2), 101.9 (C-1), 81.4 (C-3), 78.7, 75.2 (C-2, C-5), 73.8 (C-4), 74.0, 73.6, 72.6, 72.0, 71.2, 70.9, 68.7, (C-6, 6 CH_2), 42.9 (CH_2Cl).

Anal. Calcd for $C_{29}H_{37}O_7$ (533.0): C, 65.34; H, 7.00. Found: C, 65.37; H, 6.99.

Phenyl 2,3-Di-*O*-allyl-6-*O*-benzyl-4-*O*-{2-[ω-hydroxytri(oxyethylene)ethyl]}-β-D-galactopyranoside (14)

A solution of KOH (112 mg, 2.0 mmol) in diethylene glycol (6 mL) was poured into **13** (533 mg, 1.0 mmol) under vigorous stirring and the mixture was heated for about 5 h at 70 °C (TLC control). After cooling to r.t., the mixture was diluted with H_2O (10 mL), neutralised with 10% aq HCl, and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic phases were dried (Na_2SO_4), concentrated under reduced pressure and compound **14** was separated from the residue by column chromatography (Table 4).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.38−6.98 (m, 10 H, C_6H_5), 6.06−5.87 (m, 2 H, 2 CH_2CH=CH_2), 5.39−5.12 (m, 4 H, 2 CH_2CH=CH_2), 4.88 (d, 1 H, $J_{1,2}$ = 7.94 Hz, 1-H), 4.57 (dd, 2 H, J = 11.91 Hz, CH_2Ph), 4.49−4.21 (m, 4 H, 2 CH_2CH=CH_2), 4.08 (m, 1 H, 5-H), 3.91−3.47 (m, 20 H, 2-H, 4-H, 6-H, 6'-H, 8 CH_2), 3.43 (dd, 1 H, $J_{2,3}$ = 9.76, $J_{3,4}$ = 3.05 Hz, H-3).

^{13}C NMR (62 MHz, $CDCl_3$): δ = 157.5, 138.1, 129.3, 128.4, 127.8, 127.7, 122.4 (C_6H_5), 135.4, 134.9 (2 CH_2CH=CH_2), 116.7, 116.6 (2 CH_2CH=CH_2), 101.8 (C-1), 81.4 (C-3), 78.7, 75.2 (C-2, C-5), 73.9 (C-4), 73.9, 73.6, 72.5, 71.9, 70.8, 70.6, 70.5, 70.3 (10 CH_2), 68.8 (C-6), 61.7 (CH_2OH).

Anal. Calcd for $C_{33}H_{46}O_{10}$ (602.5): C, 65.76; H, 7.69. Found: C, 65.58; H, 7.73.

Phenyl 2,3-Di-*O*-allyl-6-*O*-benzyl-4-*O*-{2-[ω-hydroxypenta(oxyethylene)ethyl]}-β-D-galactopyranoside (15)

A solution of KOH (112 mg, 2.0 mmol) in tetraethylene glycol (6 mL) was poured onto **13** (533 mg, 1.0 mmol) under vigorous stirring and the mixture was heated for about 5 h at 70 °C (TLC control). The mixture was worked up as described for compound **14** yielding the syrupy product **15** after column chromatographic purification (Table 4).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.34−6.94 (m, 10 H, C_6H_5), 6.02−5.83 (m, 2 H, 2 CH_2CH=CH_2), 5.35−5.08 (m, 4 H, 2 CH_2CH=CH_2), 4.85 (d, 1 H, $J_{1,2}$ = 7.6 Hz, 1-H), 4.57, 4.53 (2 d, 2 H, J = 11.9 Hz, CH_2Ph), 4.45−4.16 (m, 4 H, 2 CH_2CH=CH_2), 4.04 (m, 1 H, 5-H), 3.86−3.54 (m, 28 H, 2-H, 4-H, 6-H, 6'-H, 12 CH_2), 3.39 (dd, 1 H, $J_{2,3}$ = 9.7, $J_{3,4}$ = 3.1 Hz, 3-H).

^{13}C NMR (62 MHz, $CDCl_3$): δ = 157.5, 138.1, 129.3, 128.4, 127.8, 127.7, 122.4, 116.9 (C_6H_5), 135.4, 134.9 (2 CH_2CH=CH_2), 116.6, 116.5 (2 CH_2CH=CH_2), 101.9 (C-1), 81.5 (C-3), 78.7, 75.2 (C-2, C-5), 73.9 (C-4), 73.9, 73.6, 72.5, 72.4, 71.9, 70.8, 70.6, 70.5, 70.3 (10 CH_2), 68.8 (C-6), 61.7 (CH_2OH).

Anal. Calcd for $C_{37}H_{54}O_{12}$ (690.8): C, 64.30; H, 7.88. Found: C, 64.16; H, 7.93.

2,3-Di-*O*-allyl-6-*O*-benzyl-1,4-*O*-(3,6,9,12,15-pentaoxaheptadecan-1,17-diyl)-β-D-galactopyranose (16)

Under argon phenyl galactoside **15** (500 mg, 0.724 mmol) was dissolved in anhyd dichloroethane (20 mL) in the presence of molecular sieve (4 Å). After cooling the mixture to −10 °C, a solution of TMSOTf (130 μL, 0.724 mmol) in anhyd CH_2Cl_2 (5 mL) was added while stirring within 15 min. (argon atmosphere). Stirring was continued at −10 °C for 1 h. Subsequently, the mixture was allowed to warm up to r.t. within 2 h. Then the reaction was terminated by the addition of $CHCl_3$ (15 mL), H_2O (5 mL) and satd aq $NaHCO_3$ solution (10 mL) while stirring vigorously (5 min.). The organic phase was separated, washed with H_2O, dried (Na_2SO_4), filtered and concentrated under reduced pressure. After column chromatographic purification **16** was isolated as a syrupy product (Table 4).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.30−7.25 (m, 5 H, C_6H_5), 6.02−5.79 (m, 2 H, 2 CH_2CH=CH_2), 5.30−5.07 (m, 4 H, 2 CH_2CH=CH_2), 4.57, 4.53 (2 d, 2 H, J = 11.9 Hz, CH_2Ph), 4.39−4.09 (m, 4 H, 2 CH_2CH=CH_2), 4.23 (d, 1 H, $J_{1,2}$ = 7.3 Hz, 1-H), 4.09−3.44 (m, 29 H, 2-H, 4-H, 5-H, 6-H, 6'-H, 12 CH_2), 3.28 (dd, 1 H, $J_{2,3}$ = 9.7, $J_{3,4}$ = 3.1 Hz, 3-H).

^{13}C NMR (62 MHz, $CDCl_3$): δ = 138.1, 128.4, 127.9, 127.7 (C_6H_5), 135.5, 135.1 (2 CH_2CH=CH_2), 116.4, 116.2 (2 CH_2CH=CH_2), 103.8 (C-1), 81.5 (C-3), 79.1, 74.8, 72.9 (C-2, C-4, C-5), 74.2, 73.9, 73.8, 72.1, 71.5, 71.4, 71.2, 71.2, 71.2, 71.1, 71.1, 71.0, 70.9, 70.8, (14 CH_2), 69.4, 68.3 (CH_2, C-6).

Anal. Calcd for $C_{31}H_{48}O_{11}$ (596.7): C, 62.38; H, 8.11. Found: C, 62.62; H, 8.11.

{[6-*O*-Benzyl-2,3-*O*-bis(diphenylphosphino)-1,4-*O*-(3,6,9-trioxaundecan-1,11-diyl)-α-D-glucopyranoside]Rh(COD)}BF_4 (18)

To a stirred solution of **8** (0.91 g, 2.1 mmol) and pyridine (0.51 mL, 6.3 mmol) in THF (10 mL) was added dropwise chlorodiphenylphosphine (0.96 g, 4.3 mmol) at 0 °C and the mixture was allowed to warm up to r.t. (inert gas atmosphere). After filtration (removal of pyridine hydrochloride), the filtrate was concentrated in vacuum and the residue dissolved in Et_2O (5 mL). The Et_2O solution was diluted with pentane (4 mL), then filtered, and concentrated. The 6-*O*-benzyl-2,3-*O*-bis(diphenylphosphino)-1,4-*O*-(3,6,9-trioxaundecan-1,11-diyl)-α-D-glucopyranoside (**17**) obtained did not crystallize. This was used as such in the next step. Under anaerobic conditions a solution of **17** in THF (5 mL) was added dropwise to a stirred solution of [Rh(COD)(acac)] (620 g, 3.0 mmol) in THF (3 mL). Subsequently, 40% aq tetrafluoroboric acid (0.25 mL) was added to the homogenous solution and complex **18** was precipitated with Et_2O, isolated by filtration, and dried in vacuum (Table 4).

^{31}P{^{1}H} NMR ($CDCl_3$): δ = 134.5 (dd, J = 180, 25 Hz) and 138.3 (dd, J = 182, 25 Hz).

Anal. Calcd for $C_{53}H_{62}BF_4O_9P_2Rh$ (1094.7): C, 58.15; H, 5.71; P, 5.66; Rh 9.40. Found: C, 54.22; H, 5.61; P, 4.80; Rh, 8.99.

6-*O*-Benzyl-2,3-*O*-bis-diphenylphosphino-1,4-*O*-(3,6,9,12-tetraoxatetradecan-1,14-diyl)-α-D -glucopyranoside (19)

To a solution of **9** (1.53 g, 3.24 mmol) and pyridine (0.72 mL, 8.9 mmol) in THF (5 mL) was added dropwise a solution of chlorodiphenylphosphine (1.43 g, 6.48 mmol) in THF (10 mL) at 0 °C while stirring (inert gas atmosphere) and the mixture was allowed to warm up to r.t. After filtration (removal of pyridine hydrochloride), the filtrate was concentrated in vacuum, the residue was treated with toluene (5 mL), filtered, and concentrated (95 % yield of crystalline **19**).

^{31}P{^{1}H} NMR (161.9 MHz, C_6D_6): δ = 110.9 (s) and 117.4 (s).

^{1}H NMR (400 MHz, C_6D_6): δ = 3.04−4.10 (m, 22 H), 4.49−4.56 (m, 2 H), 4.66 (ddd, *J* = 2.0, 2.9, 10.0 Hz), 4.80 (AB, *J* = 12.0 Hz), 4.86 (AB, *J* = 12.0 Hz), 5.15 (dd, *J* = 1.0, 3.8 Hz), 5.21 (ddd, *J* = 0.8, 9.2, 18.5 Hz), 7.09−7.85 (m, 25 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 67.97, 68.05, 69.66, 70.58, 70.64, 71.18, 71.21, 71.28, 71.32, 71.78, 71.89, 72.09, 73.74, 78.44 (d, *J* = 1.9 Hz), 80.72 (dd, *J* = 1.9, 16.2 Hz), 83.94 (d, *J* = 6.7, 19.1 Hz), 98.34 (d, *J* = 8.6 Hz), 127−133 (arom), 139.88, 142.49 (d, *J* = 13.4 Hz), 143.84 (d, *J* = 12.4 Hz), 144.42 (d, *J* = 21.9 Hz), 145.05 (d, *J* = 22.9 Hz).

{[6-*O*-Benzyl-2,3-*O*-bis(diphenylphosphino)-1,4-*O*-(3,6,9,12-tetraoxatetradecan-1,14-diyl)-α-D-glucopyranoside]Rh(COD)}BF_4 (20)

To a stirred solution of [Rh(COD)(acac)] (0.92 g 3.0 mmol) in THF (1.5 mL) was added dropwise a solution of the ligand **19** (2.52 g, 3.0 mmol) in THF (3 mL) (inert gas atmosphere). Subsequently, 40% aq tetrafluoroboric acid (0.42 mL) was added, the complex **20** was precipitated with Et_2O, separated, and dried in vacuum (Table 4).

^{31}P{^{1}H} NMR (161.9 MHz, $CDCl_3$): δ = 137.29 (dd, *J* = 180.3, 25.0 Hz) and 139.77 (dd, *J* = 181.7, 25.0 Hz),

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.36−2.54 (br m, 4 H), 2.68−2.82 (br m, 4 H), 3.30 (ABMX, J_{AB} = 11.0, *J* = 8.7, *J* = 2.0 Hz), 3.39 (ABMX, J_{AB} = 11.0, *J* = 3.6, *J* = 2.1 Hz), 3.52 (ddd, *J* = 10.4, 3.5, 2.2 Hz, 1 H), 3.56−3.92 (m, 20 H), 3.98 (t, *J* = 2.1 Hz, 1 H), 4.09 (dd, *J* = 10.9, 2.6 Hz, 1 H), 4.39 (q, *J* = 9.6 Hz, 1H), 4.55 (br dd, *J* = 14.4, 7.8 Hz), 4.63 (br dd, *J* = 15.5, 7.3 Hz), 4.69 (AB, *J* = 11.9 Hz), 4.70 (d, *J* = 4.0 Hz, 1 H), 4.80 (AB, *J* = 11.9), 4.91 (br s, 1 H), 5.07 (br s, 1 H), 7.49−8.40 (m, 25 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.92, 31.65, 31.92, 68.03, 68.77, 69.59, 70.04, 70.22, 70.47, 70.99, 71.10, 71.17, 71.38, 71.50, 72.31, 73.86, 77.15 (d, *J* = 13.4 Hz), 77.19, 80.78 (d, *J* = 11.4 Hz), 97.76 (d, *J* = 3.8 Hz), 101.68, 101.95, 108.39, 109.34, 128.14−138.23 (arom).

Anal. Calcd for $C_{55}H_{66}BF_4O_{10}P_2Rh$ (1138.8): C, 58.01; H, 5.84; P, 5.44; Rh 9.04. Found: C, 57.07; H, 5.86; P, 5.94; Rh, 8.61.

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