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TETRAHEDRON

Synthesis, Extraction Ability and Application in Asymmetric Synthesis of Azacrown Ethers Derived from D-glucose

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Abstract: A number of new chiral monoaza-15-crown-5 derivatives (**4-9**) and lariat ethers (**10-15**) anellated to phenyl-β-D-glucopyranoside have been synthesized. Their extracting ability was measured with alkali metal (Li, Na, K) and ammonium cations. The derivatives show significant asymmetric induction as phase transfer catalysts in the Michael addition of 2-nitropropane to chalcone (82% ee) although in low yield, and in the Darzens condensation of phenacyl chloride with benzaldehyde (74% ee). The substituent at the nitrogen atom of the crown ethers has a major influence on both the extraction ability and the enantioselectivity.

INTRODUCTION

One of the most attractive types of catalytic asymmetric synthesis is enantioselective induction using chiral crown ethers. Although many optically active crown ethers have been synthesized, only a few have successfully been applied as catalysts in asymmetric reactions;[1] the collection of further information is still required to obtain a better understanding of the effect of the structure of the chiral catalyst in these processes. The chiral nature of the crown ether, the rigidity of the micro-environment of its cavity and the quality of the side arm are all expected to play an important role. Azacrown ethers with a side arm attached to the nitrogen atom in the macrocyclic ring may enhance and regulate the cation binding properties as well as the lipophilicity. Lariat (lasso) ethers or armed crown ethers having heteroatom containing podand arms are known to have highly lipophilic character and a unique guest specifity via macro-ring-side arm cooperativity.[2]

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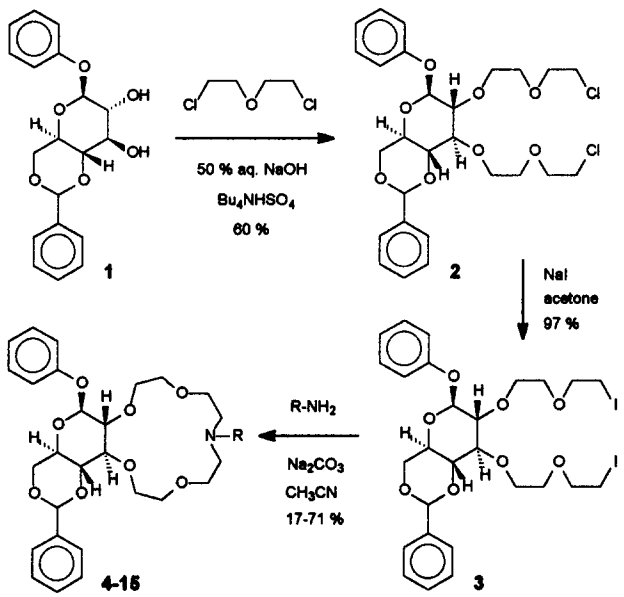
We have previously reported the synthesis and extracting ability of 15-membered ring monoaza-crown ethers and lariat ethers derived from methyl-α-D-glucopyranoside and methyl-α-D-galactopyranoside respectively.[3] These coronands have proved to be successful catalysts for an asymmetric Michael addition reaction and a Darzens condensation.[4,5] We have found that both the chemical yield and the optical purity depend on the substituent at the nitrogen atom, and the substituents of the sugar unit.

As part of a programme directed at the study of similar catalysts, we have prepared some new chiral monoaza-crown ethers and lariat ethers derived from phenyl-β-D-glucopyranoside. They possess differently structured pendant (**4-9**) or functionalized podand arms (lariat ethers **10-15**). The effects of these side arms on the extraction ability (complexing properties) and the catalysis in two chiral C-C bond forming reactions have been examined.

RESULTS AND DISCUSSION



Scheme 1

The starting protected monosaccharide, phenyl-4,6-O-benzylidene-β-D-glucopyranoside (**1**) was prepared in four steps according to the literature procedure.[7] The vicinal free hydroxy groups in compound **1** were alkylated by the method of Gross *et al.*[8] with bis(2-chloroethyl)ether as reagent and solvent. The liquid-liquid two-phase reaction using tetrabutylammonium hydrogen sulfate as phase transfer catalyst and 50% aqueous sodium hydroxide solution gave rise to the bis-chloro podand **2** (r.t., 8 h).

Exchange of the chlorines in **2** by iodines was carried out using sodium iodide in acetone (reflux, 48 h) yielding the bis-iodo derivative **3**. Compound **3** was cyclized with various primary amines: *n*-butylamine, *n*-hexylamine, 2,4-dimethyl-3-pentanamine, cyclohexylmethylamine, benzylamine, 2-phenylethylamine,

2-(2-methoxyphenyl)ethylamine, 2-(4-methoxyphenyl)ethylamine, 2-hydroxyethylamine, 2-methoxyethylamine, 3-hydroxypropylamine and 3-methoxypropylamine according to the method described previously.[3] The method requires dry Na_2CO_3 in acetonitrile as solvent (reflux, 24-48 h). In dilute solutions (1-3%) polycondensation side reactions are suppressed and the desired intramolecular cyclization reaction takes place preferably. In this way we obtained the corresponding 15-membered monoaza-crown ethers **4-15** in relatively high yields starting from **3** and the corresponding primary amine. The yields of the ring closure product, after purification by chromatography, vary from 17-71 %.

Extracting Properties

The phase transfer properties (in a liquid-liquid system) of the newly synthesized crown ethers were characterized by the extraction of picrate salts (lithium, sodium, potassium and ammonium picrate) from water into dichloromethane following the procedure described by Kimura *et al.*[9] The concentration of the picrates in water was measured by UV spectroscopy. The results are summarized in Table 1.

Table 1. Extraction of alkali metal and ammonium picrates with crown ethers

Compound	R	Extractability (%)[a]			
		Li^+	Na^+	K^+	NH_4^+
4	$CH_3(CH_2)_3$	60	63	59	76
5	$CH_3(CH_2)_5$	67	68	62	74
6	$(CH_3)_2(CH)_3(CH_3)_2$	15	47	49	56
7	$C_6H_{11}CH_2$	17	38	41	55
8	$C_6H_5CH_2$	13	24	24	33
9	$C_6H_5CH_2CH_2$	42	69	54	72
10	*o*-CH_3O-C_6H_4-CH_2CH_2	19	33	31	51
11	*p*-CH_3O-C_6H_4-CH_2CH_2	13	27	26	41
12	$HOCH_2CH_2$	14	41	39	47
13	$CH_3OCH_2CH_2$	44	72	71	76
14	$HOCH_2CH_2CH_2$	11	26	28	44
15	$CH_3OCH_2CH_2CH_2$	25	39	40	53

[a] Room temperature; aqueous phase (5 mL); [picrate] $=5*10^{-3}$ M; organic phase (CH_2Cl_2 5 mL); [crown ether] $= 1*10^{-2}$ M. Defined as % picrate extracted into the organic phase, determined by UV spectroscopy. Error = ±1%.

The data collected in Table 1 show the transferred salt amount as a percentage of the initial salt concentration (extractability %). A higher value indicates a better phase transfer capability of the crown. The strongest complexes are formed with ammonium ion presumably due to the different and stronger coronate complexation (by three H-bonds via three-point interaction) whereas alkali metal cations only have metal-oxygen coordination interaction. Not withstanding the tighter cavity of 15-crown-5, the coronands form complexes of the same strength with Na^+ and K^+, probably due to the formation of 2:1 sandwich type complexes, with exception made for compound **9** which has a phenethyl group as side arm.

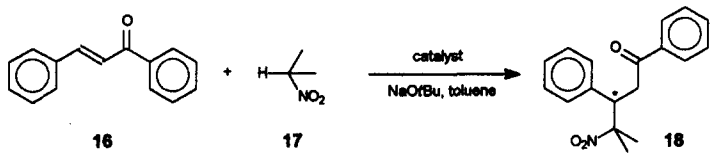
Of the crowns **4-9** lacking heteroatoms in the arm, the best extracting ability is displayed by **4** and **5**, probably because of the increased lipophilicity due to their butyl and hexyl side arms. The multi-branched arm (**6**) and the presence of the cyclohexylmethyl group (**7**) provide a weaker complexation because of steric hindrance. Benzyl substitution (**8**) lowers the extractability but the importance of the chain length of the side arm is shown by comparing **8** and **9** with the phenethyl arm extracting two, or in some cases three, times more ions. If the aromatic ring of the phenethyl arm is *ortho* or *para* substituted by a methoxy group (**9**, **10**, **11**) the extracting capability decreases significantly. This is presumably due to electronic and/or steric effects of the methoxy substituents in the interaction between the macrocyclic ring, the enfolding side arm and the cation.

Of the examined lariat ethers **12-15** compounds **12** and **14** having terminal hydroxy groups on the side arms show moderate extracting ability. The hydrophilic hydroxyl functions associated with water molecules possibly prevent the enfolding arm from participating in the complex formation. Indeed, the extracting ability increases significantly on methylation (**13**, **15**) of the hydroxy groups. The highest extraction value is displayed by coronand **13** carrying a 'methoxyethyl-lasso'; This compound has the best arm length and a flexible hydrocarbon spacer between the nitrogen atom and the effective function at the terminal.

We can conclude that the phase transfer character of the newly synthesized crown ethers (**4-15**) strongly depends on the substituent at the nitrogen atom; a heteroatom-containing terminal group attached by two carbon atom appears to be ideal (**13**). Compound **9** also proved to be a good phase transfer agent but this is probably due to π-π interactions between the aromatic systems of the phenylethyl group and the picrate.

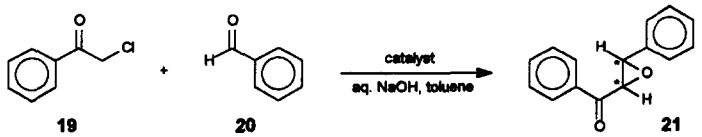
Asymmetric Induction

Compounds **4-15** were then used as chiral phase transfer catalysts. These catalysts proved to be effective in two reactions: the Michael addition of 2-nitropropane (**17**) to chalcone (**16**) (Scheme 2), and the Darzens condensation of phenacyl chloride (**19**) with benzaldehyde (**20**) (Scheme 3).



16 17 18

Scheme 2



19 20 21

Scheme 3

The Michael addition was carried out in toluene with solid sodium tertiary butoxide as base (35 mol%) and chiral catalyst (7 mol%) at room temperature. After the usual work-up procedure, the adduct

(**18**) was isolated by preparative TLC or column chromatography; the asymmetric induction, expressed in terms of the enantiomeric excess (e.e.), was monitored by measuring the optical rotation of the product **18** and comparing it with literature data for the preferred pure enantiomer and by ^{1}H NMR spectroscopy using (+)-Eu(hfc)$_3$ as chiral shift reagent. The results given in Table 2 show that the (+)-(S)-adduct **18** is always in excess and moreover that the substituent on the nitrogen atom of the catalyst has a significant influence on both the chemical yield and the asymmetric induction.

Table 2. Results of the Michael addition of 2-nitropropane to chalcone and Darzens condensation of phenacyl chloride with benzaldehyde

Entry	Catalyst	Michael addition [a]		Darzens condensation [e]	
		Yield (%)	e.e. (%) [b]	Yield (%)	e.e. (%) [b]
1	**4**	19 [c]	27	92	4
2	**5**	6	23	94	5
3	**6**	2 [d]	2	40	2
4	**7**	10	24	70	8
5	**8**	16	6	88	12
6	**9**	18	82 (80 [f])	72	30
7	**10**	61	15	65	13
8	**11**	50	25	67	33
9	**12**	12 [c]	45	87	53
10	**13**	15	66 (61 [f])	72	13
11	**14**	12	6	68	74
12	**15**	18	48 (46 [f])	75	7

[a] Reaction time 45 h; [b] Determined by optical rotation; [c] Reaction time 8 h, [d] Reaction time 90 h; [e] Reaction time 2 h; [f] Determined by ^{1}H NMR spectroscopy.

Apparently, crown ethers **4-15** are weak catalysts in this Michael addition: after relatively long reaction times (8-45 h), adduct **18** is formed with low yield (2-61%). The weakest catalyst, compound **6** (entry 3) containing a bulky alkyl side arm, provided very low chemical (2%) and optical yield (e.e.: 2%). The use of crowns **10** and **11**, having methoxyphenylethyl group gave the highest yields (61%, 50% respectively) with moderate enantiomeric excess (e.e.: 15%, 25% respectively). Lariat ethers (**12**, **13**, **15**) display greater asymmetric induction (e.e.: 45%, 66%, 48% respectively). Comparing the obtained data for the latter compounds, it is clear that the methyl ethers give rise to higher enantioselectivity (66%, 48% respectively) than their hydroxy analogues (**12**, **14**, e.e.: 45%, 6% respectively). The results for catalysts **8** and **9** possessing benzyl and phenylethyl side groups indicate the importance of the length of the side arm on the nitrogen atom, the former gives 6%, the latter 82% e.e., the best result.

In the experiments in Table 3 the influence of the reaction conditions (reaction time, temperature, base) on the reaction catalyzed by crown **9** is shown. By increasing the reaction time (entries 1-3) and the concentration (entries 10 and 11) the chemical yield increases but the enantioselectivity diminishes. The use

of low temperature produces lower chemical yields (entries 4 and 5). The application of other bases (entries 6-8) results in higher yields and the asymmetric induction is not affected considerably.

Table 3. The effect of the reaction conditions in the Michael addition of 2-nitropropane to chalcone catalyzed by crown ether **9** and **13**

Entry	Time (h)	Temp. (°C)	Catalyst	Base	Yield (%) [a]	e.e. (%) [b]
1	48	20	**9**	NaO*t*Bu	18	82 (80 [c])
2	90	20	**9**	NaO*t*Bu	36	27
3	340	20	**9**	NaO*t*Bu	60	24
4	24	-20	**9**	NaO*t*Bu	17	22
5	65	-78	**9**	NaO*t*Bu	2	11
6	40	20	**9**	NaH	48	24
7	40	20	**9**	NaOEt	60	22
8	72	20	**9**	KO*t*Bu	71	25
9	160	20	**9**	KF	71	25
10	40	20	**13**	NaO*t*Bu	15	66 (61 [c])
11 [d]	40	20	**13**	NaO*t*Bu	61	19 (16 [c])

[a] Based on isolation by column chromatography; [b] Determined by optical rotation;
[c] Determined by ^{1}H NMR spectroscopy; [d] Two times concentrated reaction mixture

The Darzens condensation of phenacyl chloride (**19**) and benzaldehyde (**20**) was carried out in a binary liquid-liquid system, using a toluene - 30% aqueous NaOH (5:1) mixture. The work-up procedure and determination of enantiomeric excess was accomplished as mentioned for the Michael addition. In all cases the epoxy ketone product **21** with a negative optical rotation was found to be in excess (Table 2). This corresponds to an absolute configuration of *2R,3S*.[10]

In this reaction crown compounds **4-15** proved to be effective phase transfer catalysts (except **6**): after 2 hour reaction, the obtained chemical yield is 65-94%. Coronands **4-7** having alkyl or cyclohexylmethyl substituents on the nitrogen atom of the crown ring did not provoke significant asymmetric induction (entries 1-4). The importance of the chain length of the side arm can be demonstrated by comparing the effects of crowns **8** (R=CH_2Ph) and **9** (R=CH_2CH_2Ph).

Compound **12**, possessing a hydroxyethyl arm gave rise to 53% e.e., but this value decreased dramatically (e.e.: 13%) when the methylated derivative (**13**) was applied. The highest asymmetric induction (e.e.: 74%) was generated by catalyst **14** (R=$(CH_2)_3OH$) with a more efficient arm length and again its methyl ether (**15**) afforded only 7% e.e. It is interesting to note that this tendancy in this liquid-liquid system is completely the opposite to that in the solid-liquid system of the Michael addition. In the toluene-water system the presence of the hydroxy group in the side arm of the catalyst is clearly beneficial.

In the demonstrated model reactions a C-H acidic compound is being deprotonated by a suitably chosen base generating a reactive anion in the presence of the chiral crown compound. When the base is added to the reaction mixture in solid form, it is soluble in the apolar solvent only to such an extent that the complexation with the crown occurs (solid-liquid phase transfer mechanism). It is followed by deprotonation

of the C-H acidic compound and reaction with the other reactant, all occuring in the chiral niche of the solubilizing crown which results in asymmetric induction.

In conclusion, no definite relation was found between the salt extracting ability (complex formation) of the synthesized coronands and their activity in the model asymmetric reactions. In a water-dichloromethane system the best exracting ability is related to the crown ethers having butyl and hexyl group on the nitrogen atom of the macrocyclic ring. On the other hand, these compounds proved to be ineffectual phase transfer catalysts in the solid-liquid system of the Michael addition. Compound **9** with a phenethyl substituent and compounds **13** and **15** with methoxyethyl and methoxypropyl podand arms showed the highest chiral induction but with low yields. In the Darzens condensation, satisfactory chemical yields were obtained in a liquid-liquid system; compounds **12** and **14** with hydroxyethyl and hydroxypropyl arms were the most effective catalysts with respect to enantioselectivity. We have proved that the substituents on the nitrogen atom had distinct importance in the asymmetric induction: the lariat ethers were good in both model reactions, probably due to the assistance of the heteroatom in the enfolding podand arm in cation complexation when a three-dimensional complex is formed improving the phase transfer process as well as the asymmetric induction.

EXPERIMENTAL

General. ^{1}H NMR (500, 400 and 250 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on Bruker AMX 400 (^{13}C) and Bruker WM 250 instruments in $CDCl_3$. DEPT (Distortionless enhancement by polarization transfer) and ^{13}C- ^{1}H correlation experiments (1D and 2D) were used for signal assignment. The mass spectra were obtained on a Kratos MS50TC instrument using DS90 data system. Chemical ionization was applied as ionization technique. Optical rotation was measured on a Perkin Elmer 241 polarimeter and on a Propol automatic polarimeter at 20 °C. Analytical and preparative thin layer chromatography was performed on silica gel (60 PF-224, Merck) and on aluminium oxide (F-254, Riedel-de-Haën, 60 PF-254 (Typ E), Merck) TLC plates. Column chromatography was carried out using 70-230 mesh silica gel (E. M. Merck) and 100-125 mesh aluminum oxide (Fluka). Melting point measurements were taken on a Büchi 510 and an electrothermal IA 9000 apparatus. Elemental analysis was performed on a Perkin Elmer 240 automatic analyzer.

The starting phenyl-4,6-O-benzylidene-β-D-glucopyranoside (**1**) was synthesized as described.[7]

Phenyl-4,6-*O*-benzylidene-2,3-bis[(2-chloroethoxy)ethyl]-β-D-glucopyranoside (2) (Scheme 1). A solution of 10.0 g (29.1 mmol) of compound **1** and 9.85 g (29.1 mmol) of tetrabutylammonium hydrogen sulfate in 73 mL (623 mmol) of bis(2-chloroethyl)ether was vigorously stirred with 109 mL of 50% NaOH solution at room temperature for 8 h. A mixture of 300 mL CH_2Cl_2 and 300 mL water was added to the reaction mixture. The organic layer was decanted and the aqueous one was washed with CH_2Cl_2. The organic phases were combined and washed with water, dried with $MgSO_4$, filtered and concentrated under vacuum. After the removal of the solvent and the bis(2-chloroethyl)ether, the product was purified by column chromatography on silica gel using hexane-ethyl acetate (80:20) as eluent to give 9.8 g (60.5%) of **2** as a white solid; M.p.: 74-75 °C (ethanol); $[\alpha]_D$ -37.8° (c 1, $CHCl_3$); IR (KBr, cm^{-1}): 2904, 1600, 1496, 1364, 1242,

1142, 1093, 1022, 748, 695, 653; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 3.45-3.60 (m, 6H, H-2, H-5 and 2 CH_2 of the podand arm), 3.60-3.75 (m, 10H, H-3, H-4 and 4 CH_2 of the podand arm), 3.79 (t, 1H, *J*=10.5 Hz, H-6), 3.92-4.12 (m, 4H, 2 OCH_2 of the podand arm), 4.37 (dd, 1H, *J*=10.5 Hz, 5Hz, H-6), 5.05 (d, 1H, *J*=7.6 Hz, H-1), 5.55 (s, 1H, PhCH), 7.00-7.10 (m, 3H, OPhH-*o* and OPhH-*p*), 7.30 (tm, 2H, *J*=7.4 Hz, OPhH-*m*), 7.37-7.43 (m, 3H, CHPhH-*m*-*p*), 7.49 (dm, 2H, *J*=7.6 Hz, CHPhH-*o*); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 42.6, 42.7 (2 CH_2Cl), 66.2 (C-5), 68.7 (C-6), 70.7, 70.8, 71.1, 71.2, 72.4, 72.5 (6 OCH_2 of the podand arm) 80.7 (C-3), 81.7 (C-4), 82.5 (C-5), 101.4 (PhCH), 101.9 (C-1), 117.0 (2 OPhC-*o*), 123.0 (OPhC-*p*), 126.0 (2 CHPhC-*o*), 128.2 (2 CHPhC-*m*), 129.0 (CHPhC-*p*), 129.6 (2 OPhC-*m*), 137.3 (CHPhC-*ipso*), 157.1 (OPhC-*ipso*) ; MS, m/z: 557 [M^++1] (6), 463 (20) 339 (88), 233 (27), 183 (100). Anal. Calcd for $C_{27}H_{34}O_8Cl_2$: C, 58.17; H, 6.15; Cl, 12.72. Found: C, 58.21; H, 6.12; Cl, 12.50.

Phenyl-4,6-*O*-benzylidene-2,3-bis[(2-iodoethoxy)ethyl]-β-D-glucopyranoside (3) (Scheme 1). A mixture of 10.0 g (18 mmol) of bis-chloro derivative **2** and 10.8 g (72 mmol) of dry NaI in 200 mL of dry acetone was stirred under reflux for 48 h. After cooling the precipitate was filtered and washed with acetone. The combined acetone solution was evaporated under vacuum. The residue was dissolved in 100 mL of CH_2Cl_2, washed with water, and dried over Na_2SO_4 to give **3** (12.9 g, 97.2%) as a white solid; M.p.: 58 °C; $[\alpha]_D$ -25.2° (c 1, $CHCl_3$); IR (KBr, cm^{-1}): 2879, 1601, 1590, 1494, 1370, 1236, 1088, 1007, 744, 690; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.19 (t, 4H, *J*=7 Hz, 2 CH_2I), 3.45-3.58 (m, 2H, H-2 and H-5), 3.60-3.75 (m, 10H, H-3, H-4 and 8 podand arm-H), 3.79 (t, 1H, *J*=10.5 Hz, H-6), 3.93-4.12 (m, 4H, 4 podand arm-H), 4.36 (dd, 1H, *J*=10.5, 5 Hz, H-6), 5.06 (d, 1H, *J*=7.6 Hz, H-1), 5.56 (s, 1H, PhCH), 7.00-7.10 (m, 3H, OPhH-*o* and OPhH-*p*), 7.30 (tm, 2H, *J*=7.4 Hz, OPhH-*m*), 7.37-7.43 (m, 3H, CHPhH-*m*-*p*), 7.49 (dm, 2H, *J*=7.6 Hz, CHPhH-*o*); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 2.8, 3.0 (2 CH_2I), 66.2 (C-5), 68.7 (C-6), 70.3, 70.4, 71.8, 71.9, 72.5, 72.6 (6 OCH_2 of the podand arm), 80.7 (C-3), 81.7 (C-4), 82.5 (C-5) 101.4 (PhCH), 101.9 (C-1), 117.0 (2 OPhC-*o*), 123.0 (OPhC-*p*), 126.0 (2 CHPhC-*o*), 128.2 (2 CHPhC-*m*), 129.0 (CHPhC-*p*), 129.6 (2 OPhC-*m*), 137.3 (CHPhC-*ipso*), 157.1 (OPhC-*ipso*); MS, m/z: 741 [M^++1] (3), 647 (13), 541 (11), 431 (40), 305 (38), 183 (100). Anal. Calcd for $C_{27}H_{34}O_8I_2$: C, 43.80; H, 4.63; I, 34.28. Found: C, 43.70; H, 4.51; I, 34.21. The resulting compound was used without further purification.

General method for preparation of crown ethers **4-15**. 3.84 g (36.2 mmol) of dry Na_2CO_3 was suspended in a solution of 4.60 mmol of the corresponding primary amine and 3.45 g (4.6 mmol) of bis-iodo compound **3** in 100 mL of dry acetonitrile under argon. The stirred reaction mixture was refluxed for 24-48 h and monitored by TLC until the disappearance of the bis-iodo compound. After cooling the precipitate was filtered and washed with acetonitrile. The combined acetonitrile solution was concentrated at reduced pressure. The residue oil was dissolved in $CHCl_3$, washed with water and dried over Na_2SO_4 and the solvent evaporated under vacuum. The corresponding monoaza-crown ether was isolated by column chromatography or preparative TLC using silica gel or aluminium oxide.

Phenyl-4,6-*O*-benzylidene-2,3-dideoxy-β-D-glucopyranosido[2,3-*b*]-*N*-butyl-1,4,7,10-tetraoxa-13-azacyclopentadecane (4). The purification was carried out by column chromatography with eluent $CHCl_3$:MeOH:NH_4OH = 97:2:1 on silica gel. Yield: 43.9 %; faint yellow crystals; M.p.: 105-106°C (ethanol); $[\alpha]_D$ -43.0° (c 1, $CHCl_3$); IR (KBr, cm^{-1}): 2926, 2869, 1600, 1491, 1368, 1228, 1093, 1031, 749, 693; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.90 (t, 3H, *J*=7.3 Hz, CH_3), 1.30 (m, 2H, *J*=7.2 Hz, $NCH_2CH_2CH_2$), 1.44 (m, 2H, *J*=7.6 Hz, $NCH_2CH_2CH_2$), 2.48 (t, 2H, *J*=7.4 Hz,

$NCH_2CH_2CH_2$), 2.65-2.88 (m, 4H, 2 NCH_2 of the macrocycle), 3.43-3.83 (m, 12H, H-2, H-3, H-4, H-5 and 4 OCH_2 of the macrocycle), 3.79 (t, 1H, *J*=10.5 Hz, H-6), 3.95-4.14 (m, 4H, 2 OCH_2 of the macrocycle), 4.36 (dd, 1H, *J*=10.5, 5 Hz, H-6), 5.06 (d, 1H, *J*=7.6 Hz, H-1), 5.54 (s, 1H, PhCH), 7.02 (dm, 2H, *J*=7.7 Hz, OPhH-*o*), 7.05 (tm, 1H, *J*=7.2 Hz, OPhH-*p*), 7.30 (tm, 2H, *J*=8.0 Hz, OPhH-*m*), 7.33-7.40 (m, 3H, CHPhH-*m*-*p*), 7.47 (dm, 2H, *J*=7.7 Hz, CHPhH-*o*); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 14.0, 20.6, 29.6 ($CH_3CH_2CH_2$), 54.0, 54.1 (2 NCH_2 of the macrocycle), 56.5, (NCH_2), 66.1 (C-5), 68.7 (C-6), 69.2, 69.3, 70.3, 70.4, 72.4, 72.5 (6 OCH_2 of the macrocycle), 81.0, 81.5 (C-3, C-4), 81.7 (C-2), 101.2 (PhCH), 102.2 (C-1), 117.0 (2 OPhC-*o*), 123.0 (OPhC-*p*), 126.0 (2 CHPhC-*o*), 128.2 (2 CHPhC-*m*), 129.0 (CHPhC-*p*), 129.6 (2 OPhC-*m*), 137.3 (CHPhC-*ipso*), 157.1 (OPhC-*ipso*); MS, m/z: 558 [M^++1] (100), 514 (8), 464 (33). Anal. Calcd for $C_{31}H_{43}O_8N$: C, 66.77; H, 7.77; N, 2.51. Found: C, 66.80; H, 7.71; N, 2.55.

Phenyl-4,6-*O*-benzylidene-2,3-dideoxy-β-D-glucopyranosido[2,3-*h*]-*N*-hexyl-1,4,7,10-tetraoxa-13-azacyclopentadecane (5). The purification was carried out by column chromatography with eluent $CHCl_3$:MeOH:NH_4OH = 95:5:1 on silica gel. Yield: 39.3%; light yellow oil; $[\alpha]_D$= -39.2° (c 1, $CHCl_3$); IR (KBr, cm^{-1}): 2926, 2872, 1600, 1491, 1368, 1233, 1093, 1030, 750, 696: ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.88 (t, 3H, *J*=6.6 Hz, $N(CH_2)_5CH_3$), 1.20-1.50 (m, 8H, $NCH_2(CH_2)_4CH_3$), 2.47 (t, 2H, *J*=7.5 Hz, $NCH_2(CH_2)_4CH_3$), 2.67-2.88 (m, 4H, 2 NCH_2 of the macrocycle), 3.44-3.85 (m, 12H, H-2, H-3, H-4, H-5 and 4 OCH_2 of the macrocycle), 3.79 (t, 1H, *J*=10.5 Hz, H-6), 3.95-4.14 (m, 4H, 2 OCH_2 of the macrocycle), 4.36 (dd, 1H, *J*=10.5, 5 Hz, H-6), 5.06 (d, 1H, *J*=7.6 Hz, H-1), 5.54 (s, 1H, PhCH), 7.02 (dm, 2H, *J*=7.7 Hz, OPhH-*o*), 7.05 (tm, 1H, *J*=7.2 Hz, OPhH-*p*), 7.30 (tm, 2H, *J*=8.0 Hz, OPhH-*m*), 7.33-7.40 (m, 3H, CHPhH-*m*-*p*), 7.47 (dm, 2H, *J*=7.7 Hz, CHPhH-*o*); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 14.0 ($N(CH_2)_5CH_3$), 22.6, 27.1, 27.4, 31.8 ($NCH_2(CH_2)_4CH_3$), 54.0, 54.1 (2 NCH_2 of the macrocycle), 56.8 ($NCH_2(CH_2)_4CH_3$), 66.1 (C-5), 68.7 (C-6), 69.2, 69.3, 70.3, 70.4, 72.4, 72.5 (6 OCH_2 of the macrocycle), 81.0, 81.5 (C-3, C-4), 81.7 (C-2), 101.2 (PhCH), 102.2 (C-1), 117.0 (2 OPhC-*o*), 123.0 (OPhC-*p*), 126.0 (2 CHPhC-*o*), 128.2 (2 CHPhC-*m*), 129.0 (CHPhC-*p*), 129.6 (2 OPhC-*m*), 137.3 (CHPhC-*ipso*), 157.1 (OPhC-*ipso*); MS, m/z: 586 [M^++1] (100), 514 (12), 492 (34). Anal. Calcd for $C_{33}H_{47}O_8N$: C, 67.67; H, 8.09; N, 2.39. Found: C, 67.70; H, 8.15; N, 2.30.

Phenyl-4,6-*O*-benzylidene-2,3-dideoxy-β-D-glucopyranosido[2,3-*h*]-*N*-3-(2,4-dimethyl)pentyl-1,4,7,10-tetraoxa-13-azacyclopentadecane (6). The purification was carried out by column chromatography with eluent CH_2Cl_2:MeOH = 97:3 on silica gel or preparative TLC with eluent CH_2Cl_2:MeOH = 90:10 on silica gel. Yield: 17.7%; light yellow oil; $[\alpha]_D$ -35.4° (c 1, $CHCl_3$); IR (KBr, cm^{-1}): 2926, 2870, 1600, 1491, 1368, 1230, 1093, 1030, 750, 696; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.84-0.95 (4d, 12H, *J*=6-7 Hz, 4 CH_3CH), 1.80-1.98 (m, 3H, 2 CH and 1 NCH), 2.80-2.97 (m, 4H, 2 NCH_2 of the macrocycle), 3.43-3.73 (m, 12H, H-2, H-3, H-4, H-5 and 4 OCH_2 of the macrocycle), 3.78 (t, 1H, *J*=10.5 Hz, H-6), 3.94-4.17 (m, 4H, 2 OCH_2 of the macrocycle), 4.35 (dd, 1H, *J*=10.5, 5 Hz, H-6), 5.06 (d, 1H, *J*=7.6 Hz, H-1), 5.54 (s, 1H, PhCH), 7.02 (dm, 2H, *J*=7.7 Hz, OPhH-*o*), 7.05 (tm, 1H, *J*=7.2 Hz, OPhH-*p*), 7.30 (tm, 2H, *J*=8.0 Hz, OPhH-*m*), 7.33-7.40 (m, 3H, CHPhH-*m*-*p*), 7.47 (dm, 2H, *J*=7.7 Hz, CHPhH-*o*); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 19.3, 20.4, 21.3, 21.5 (4 CH_3), 29.2, 29.4 (*C*HCH*C*H) 54.8, 55.2 (2 NCH_2 of the macrocycle), 66.0 (C-5), 68.6 (C-6), 69.9, 70.2, 71.6, 72.0, 72.3, 72.4 (6 OCH_2 of the macrocycle), 75.7 (CH*C*HCH), 80.7, 81.4, 81.5 (C-2, C-3, C-4), 101.1 (PhCH), 102.1 (C-1), 117.0 (2 OPhC-*o*), 123.0 (OPhC-*p*), 126.0 (2 CHPhC-*o*), 128.2 (2 CHPhC-*m*), 129.0 (CHPhC-*p*), 129.6 (2 OPhC-*m*), 137.3 (CHPhC-*ipso*), 157.1 (OPhC-*ipso*); MS, m/z: 600 [M^++1] (100), 556 (38), 506 (18). Anal. Calcd for $C_{34}H_{49}O_8N$: C, 68.09; H, 8.23; N, 2.33. Found: C, 68.12; H, 8.13; N, 2.30.

Phenyl-4,6-*O*-benzylidene-2,3-dideoxy-β-D-glucopyranosido[2,3-*h*]-*N*-cyclohexylmethyl-1,4,7,10-tetraoxa-13-azacyclopentadecane (**7**). The purification was carried out by column chromatography with eluent CH_2Cl_2:MeOH = 93:7 on silica gel. Yield: 32.2%; faint yellow crystals; M.p.: 104 °C (ethanol); $[\alpha]_D$ -41.1° (c 1, $CHCl_3$); IR (KBr, cm^{-1}): 2923, 2871, 1600, 1493, 1456, 1349, 1240, 1132, 1086, 1008, 963, 754, 690; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.82-1.85 (m, 11H, cyclohex-H), 2.24 (d, 2H, *J*=7.0 Hz, NCH_2cyclohex), 2.60-2.85 (m, 4H, 2 NCH_2 of the macrocycle), 3.44-3.72, 3.73-3.85 (m, 12H, H-2, H-3, H-4, H-5, 4 OCH_2 of the macrocycle), 3.79 (t, 1H, *J*=10.5 Hz, H-6), 3.93-4.13 (m, 4H, 2 OCH_2 of the macrocycle), 4.36 (dd, 1H, *J*=10.5, 5 Hz, H-6), 5.06 (d, 1H, *J*=7.6 Hz, H-1), 5.54 (s, 1H, PhCH), 7.02 (dm, 2H, *J*=7.7 Hz, OPhH-*o*), 7.05 (tm, 1H, *J*=7.2 Hz, OPhH-*p*), 7.30 (tm, 2H, *J*=8.0 Hz, OPhH-*m*), 7.33-7.40 (m, 3H, CHPhH-*m-p*), 7.47 (dm, 2H, *J*=7.7 Hz, CHPhH-*o*); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 26.1, 26.2 (2 cyclohex CH_2-β), 26.9 (cyclohex CH2-γ), 31.7, 31.8 (2 cyclohex CH2-α), 36.4 (cyclohex CH), 54.8, 54.9 (2 NCH_2 of the macrocycle), 63.8 (NCH_2cyclohex), 66.1 (C-5), 68.7 (C-6), 69.2, 69.3, 70.2, 70.3, 72.4, 72.5 (6 OCH_2 of the macrocycle), 81.1, 81.5 (C-3, C-4), 81.8 (C-2), 101.2 (PhCH), 102.2 (C-1), 117.0 (2 OPhC-*o*), 123.0 (OPhC-*p*), 126.0 (2 CHPhC-*o*), 128.2 (2 CHPhC-*m*), 129.0 (CHPhC-*p*), 129.6 (2 OPhC-*m*), 137.3 (CHPhC-*ipso*), 157.1 (OPhC-*ipso*); MS, m/z: 598 [M^++1] (100), 514 (31), 504 (35). Anal. Calcd for $C_{34}H_{47}O_8N$: C, 68.32; H, 7.92; N, 2.34. Found: C, 68.37; H, 7.85; N, 2.28.

Phenyl-4,6-*O*-benzylidene-2,3-dideoxy-β-D-glucopyranosido[2,3-*h*]-*N*-benzyl-1,4,7,10-tetraoxa-13-aza-cyclopentadecane (**8**). The purification was carried out by column chromatography with eluent $CHCl_3$:MeOH = 95:5 on silica gel or with eluent CH_2Cl_2:MeOH = 99.6:0.4 on aluminium oxide. Yield: 42.6%; light yellow oil; $[\alpha]_D$ -34.9° (c 1, $CHCl_3$); IR (KBr, cm^{-1}): 2926, 2873, 1599, 1491, 1457, 1234, 1093, 1028, 962, 750, 695; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.72-2.95 (m, 4H, 2 NCH_2 of the macrocycle), 3.45-3.85 (m, 14H, H-2, H-3, H-4, H-5, NCH_2Ph and 4 OCH_2 of the macrocycle), 3.79 (t, 1H, *J*=10.5 Hz, H-6), 3.95-4.15 (m, 4H, 2 OCH_2 of the macrocycle), 4.36 (dd, 1H, *J*=10.5, 5 Hz, H-6), 5.06 (d, 1H, *J*=7.6 Hz, H-1), 5.54 (s, 1H, PhCH), 7.02 (dm, 2H, *J*=7.6 Hz, OPhH-*o*), 7.05 (tm, 1H, *J*=7.4 Hz, OPhH-*p*), 7.19-7.41 (m, 10H, OPhH-*m*, CH_2PhH-*o-p-m*, CHPhH-*m-p*), 7.47 (dm, 2H, *J*=7.6 Hz, CHPhH-*o*); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 53.8, 53.9 (2 NCH_2 of the macrocycle), 60.7 (NCH_2Ph), 66.1 (C-5), 68.7 (C-6), 69.0, 69.1, 70.2, 70.3, 72.4, 72.5 (6 OCH_2 of the macrocycle), 81.0, 81.5 (C-3, C-4), 81.8 (C-2), 101.2 (PhCH), 102.2 (C-1), 117.0 (2 OPhC-*o*), 123.0 (OPhC-*p*), 126.0 (2 CHPhC-*o*), 126.9 (CH_2PhC-*p*), 128.1 (2 CHPhC-*m*), 128.2 (2 CH_2PhC-*m*), 128.8 (2 CH_2PhC-*o*), 129.0 (CHPhC-*p*), 129.6 (2 OPhC-*m*), 137.3 (CHPhC-*ipso*), 139.6 (CH_2PhC-*ipso*), 157.1 (OPhC-*ipso*); MS, m/z: 592 [M^++1] (100), 514 (14), 498 (37). Anal. Calcd for $C_{34}H_{41}O_8N$: C, 69.02; H, 6.98; N, 2.37. Found: C, 68.90; H, 6.92; N, 2.31.

Phenyl-4,6-*O*-benzylidene-2,3-dideoxy-β-D-glucopyranosido[2,3-*h*]-*N*-(2-phenyl)ethyl-1,4,7,10-tetraoxa-13-azacyclopentadecane (**9**). The purification was carried out by column chromatography, gradient elution with CH_2Cl_2:EtOAc:NH_4OH = 92:7:1 → 90:9:1 on silica gel or with eluent CH_2Cl_2:MeOH = 99.5:0.5 on aluminium oxide. Yield: 71%; white crystals; M.p.: 160 °C (ethanol); $[\alpha]_D$ -44.3° (c 1, $CHCl_3$); IR (KBr, cm^{-1}): 2913, 2866, 1600, 1492, 1368, 1230, 1127, 1092, 1010, 751, 694; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.77 (s, 4H, $PhCH_2CH_2$, accidental equiv.), 2.76-2.95 (m, 4H, 2 NCH_2 of the macrocycle), 3.50 (m, 1H, H-5), 3.52 (t, 1H, *J*=8 Hz, H-2), 3.67 (m, 1H, H-3

or H-4), 3.79 (t, 1H, *J*=10.5 Hz, H-6), 3.45-3.85 (m, 9H, 4 OCH_2 of the macrocycle and H-3 or H-4), 3.95-4.15 (m, 4H, 2 OCH_2 of the macrocycle), 4.36 (dd, 1H, *J*=10.5, 5 Hz, H-6), 5.06 (d, 1H, *J*=7.6 Hz, H-1), 5.54 (s, 1H, PhCH), 7.02 (dm, 2H, *J*=7.6 Hz, OPhH-*o*), 7.05 (tm, 1H, *J*=7.4 Hz, OPhH-*p*), 7.15-7.21 (m, 3H, CH_2PhH-*o*-*p*), 7.26 (tm, 2H, *J*=7.6 Hz, CH_2PhH-*m*), 7.30 (tm, 2H, *J*=7.5 Hz, OPhH-*m*), 7.33-7.40 (m, 3H, CHPhH-*m*-*p*), 7.47 (dm, 2H, *J*=7.6 Hz, CHPhH-*o*); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 34.0 (NCH_2CH_2Ph), 54.1, 54.2 (2 NCH_2 of the macrocycle), 58.7 (NCH_2CH_2Ph), 66.1 (C-5), 68.7 (C-6), 69.2, 69.3, 70.3, 70.4, 72.4, 72.5 (6 OCH_2 of the macrocycle), 81.0, 81.5 (C-3, C-4), 81.7 (C-2), 101.2 (PhCH), 102.2 (C-1), 117.0 (2 OPhC-*o*), 123.0 (OPhC-*p*), 125.9 (CH_2PhC-*p*), 126.0 (2 CHPhC-*o*), 128.2 (2 CHPhC-*m*), 128.3 (2 CH_2PhC-*m*), 128.7 (2 CH_2PhC-*o*), 129.0 (CHPhC-*p*), 129.6 (2 OPhC-*m*), 137.3 (CHPhC-*ipso*), 140.5 (CH_2PhC-*ipso*), 157.1 (OPhC-*ipso*); MS, m/z: 606 [M^++1] (100), 514 (49). Anal. Calcd for $C_{35}H_{43}O_8N$: C, 69.40; H, 7.15; N, 2.31. Found: C, 69.45; H, 7.22; N, 2.30.

Phenyl-4,6-*O*-benzylidene-2,3-dideoxy-β-D-glucopyranosido[2,3-*h*]-*N*-2-(2-methoxyphenyl)ethyl-1,4,7,10-tetraoxa-13-azacyclopentadecane (10). The purification was carried out by column chromatography with eluent CH_2Cl_2:MeOH = 95:5 on silica gel or preparative TLC with eluent CH_2Cl_2:MeOH = 99.3:0.7 on aluminium oxide. Yield: 52.6%; faint yellow crystals; M.p.: 134 °C (ethanol); $[\alpha]_D$ -43.5° (c 1, $CHCl_3$); IR (KBr, cm^{-1}): 2920, 2862, 2360, 1599, 1383, 1243, 1093, 752, 692; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.67-2.98 (m, 8H, $PhCH_2CH_2$ and 2 NCH_2 of the macrocycle), 3.44-3.85 (m, 16H, CH_2PhOCH_3, H-2, H-3, H-4, H-5, H-6 and 4 OCH_2 of the macrocycle), 3.95-4.15 (m, 4H, 2 OCH_2 of the macrocycle), 4.36 (dd, 1H, *J*=10.5, 5 Hz, H-6), 5.06 (d, 1H, *J*=7.6 Hz, H-1), 5.54 (s, 1H, PhCH), 6.82 (dm, 1H, *J*=8.1 Hz, CH_2PhH-*m*), 6.86 (tm, 1H, *J*=7.5 Hz, CH_2PhH-*m*), 7.02 (dm, 2H, *J*=7.9 Hz, OPhH-*o*), 7.05 (tm, 1H, *J*=7.4 Hz, OPhH-*p*), 7.13 (dm, 1H, *J*=7.4 Hz, CH_2PhH-*o*), 7.16 (tm, 1H, *J*=7.2 Hz, CH_2PhH-*p*), 7.30 (tm, 2H, *J*=7.7 Hz, OPhH-*m*), 7.33-7.40 (m, 3H, CHPhH-*m*-*p*), 7.47 (m, 2H, CHPhH-*o*); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 28.2 ($NCH_2CH_2PhOCH_3$), 53.9, 54.0 (2 NCH_2 of the macrocycle), 55.2 ($NCH_2CH_2PhOCH_3$), 56.7 ($NCH_2CH_2PhOCH_3$), 66.1 (C-5), 68.7 (C-6), 69.3, 69.4, 70.3, 70.4, 72.4, 72.5 (6 OCH_2 of the macrocycle), 81.0, 81.5 (C-3, C-4), 81.8 (C-2), 101.2 (PhCH), 102.2 (C-1), 110.2 (CH_2PhC-*m(3)*), 117.0 (2 OPhC-*o*), 120.4 (CH_2PhC-*m(5)*), 123.0 (OPhC-*p*), 126.0 (2 CHPhC-*o*), 127.2 (CH_2PhC-*p*), 128.2 (2 CHPhC-*m*), 128.8 (CH_2PhC-*ipso*), 129.0 (CHPhC-*p*), 129.6 (2 OPhC-*m*), 130.3 (CH_2PhC-*o(6)*), 137.3 (CHPhC-*ipso*), 157.1 (OPhC-*ipso*); 157.5 (CH_2PhC-*o(2)*); MS, m/z: 636 [M^++1] (100), 542 (24), 514 (40). Anal. Calcd for $C_{36}H_{45}O_9N$: C, 68.01; H, 7.13; N, 2.20. Found: C, 68.11; H, 7.20; N, 2.12.

Phenyl-4,6-*O*-benzylidene-2,3-dideoxy-β-D-glucopyranosido[2,3-*h*]-*N*-2-(4-methoxyphenyl)ethyl-1,4,7,10-tetraoxa-13-azacyclopentadecane (11). The purification was carried out by column chromatography with eluent CH_2Cl_2:MeOH = 94:6 on silica gel or preparative TLC with eluent CH_2Cl_2:MeOH = 99.3:0.7 on aluminium oxide. Yield: 47.6%; faint yellow crystals; M.p.: 124-125 °C (ethanol); $[\alpha]_D$ -41.1° (c 1, $CHCl_3$); IR (KBr, cm^{-1}): 2920, 2876, 1600, 1512, 1250, 1123, 1093, 823, 748, 696; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.72 (s, 4H, $PhCH_2CH_2$, accidental equiv.), 2.75-2.96 (m, 4H, 2 NCH_2 of the macrocycle), 3.44-3.84 (m, 16H, CH_2PhOCH_3, H-2, H-3, H-4, H-5, H-6 and 4 OCH_2 of the macrocycle), 3.95-4.13 (m, 4H, 4 OCH_2 of the macrocycle), 4.35 (dd, 1H, *J*=10.5, 5 Hz, H-6), 5.06 (d, 1H, *J*=7.6 Hz, H-1), 5.54 (s, 1H, PhCH), 6.81 (d, 2H, *J*=8.6Hz, CH_2PhH-m), 7.02 (dm, 2H, *J*=7.7 Hz, OPhH-*o*), 7.05 (tm, 1H, *J*=7.4 Hz, OPhH-*p*), 7.10 (d, 2H, *J*=8.6Hz, CH_2PhH-o), 7.30 (tm, 2H, *J*=8.0 Hz, OPhH-*m*), 7.33-7.40 (m, 3H, CHPhH-*m*-*p*), 7.47 (dm, 2H, *J*=7.7 Hz, CHPhH-*o*); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 33.1

($NCH_2CH_2PhOCH_3$), 54.0, 54.1, (2 NCH_2 of the macrocycle), 55.2 ($NCH_2CH_2PhOCH_3$), 58.8 ($NCH_2CH_2PhOCH_3$), 66.1 (C-5), 68.7 (C-6), 69.2, 69.3, 70.3, 70.4, 72.3, 72.4 (6 OCH_2 of the macrocycle), 81.0, 81.5 (C-3, C-4), 81.7 (C-2), 101.2 (PhCH), 102.1 (C-1), 113.7 (2 CH_2PhC-m), 117.0 (2 OPhC-*o*), 123.0 (OPhC-*p*), 126.0 (2 CHPhC-*o*), 128.2 (2 CHPhC-m), 129.0 (CHPhC-*p*), 129.5 (2 CH_2PhC-o), 129.6 (2 OPhC-*m*),), 132.5 (CH_2PhC-ipso), 137.2 (CHPhC-*ipso*), 157.1 (OPhC-*ipso*); 157.8 (CH_2PhC-*p*); MS, m/z: 636 [M^++1] (100), 542 (24), 514 (40). Anal. Calcd for $C_{36}H_{45}O_9N$: C, 68.01; H, 7.13; N, 2.20. Found: C, 68.10; H, 7.17; N, 2.17.

Phenyl-4,6-*O*-benzylidene-2,3-dideoxy-β-D-glucopyranosido[2,3-*h*]-*N*-hydroxyethyl-1,4,7,10-tetraoxa-13-azacyclopentadecane (12). The purification was carried out by column chromatography with eluent $CHCl_3$:MeOH:NH_4OH = 94:5:1 on silica gel. Light yellow oil. Yield: 48.0%; $[\alpha]_D$ -35.2° (c 1, $CHCl_3$); IR (KBr, cm^{-1}): 3180-3600, 2920, 2875, 1600, 1491, 1236, 1093, 754, 694; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.63-2.87 (m, 6H, 3 NCH_2), 3.45-3.83 (m, 15H, H-2, H-3, H-4, H-5, H-6, CH_2OH and 4 OCH_2 of the macrocycle), 3.92-4.08 (m, 4H, 2 OCH_2 of the macrocycle), 4.35 (dd, 1H, *J*=10.5, 5 Hz, H-6), 5.06 (d, 1H, *J*=7.6 Hz, H-1), 5.54 (s, 1H, PhCH), 7.02 (dm, 2H, *J*=7.7 Hz, OPhH-*o*), 7.05 (tm, 1H, *J*=7.2 Hz, OPhH-*p*), 7.30 (tm, 2H, *J*=8.0 Hz, OPhH-*m*), 7.33-7.40 (m, 3H, CHPhH-*m*-*p*), 7.47 (dm, 2H, *J*=7.7 Hz, CHPhH-*o*); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 55.0, 55.1 (2 NCH_2 of the macrocycle), 57.5, (NCH_2), 59.2 (CH_2OH), 66.0 (C-5), 68.7 (C-6), 69.2, 69.3, 70.3, 70.4, 72.3, 72.4 (6 OCH_2 of the macrocycle), 80.9, 81.5 (C-3, C-4), 81.8 (C-2), 101.2 (PhCH), 102.1 (C-1), 117.0 (2 OPhC-*o*), 123.0 (OPhC-*p*), 126.0 (2 CHPhC-*o*), 128.2 (2 CHPhC-*m*), 129.0 (CHPhC-*p*), 129.6 (2 OPhC-*m*), 137.3 (CHPhC-*ipso*), 157.1 (OPhC-*ipso*); MS, m/z: 546 [M^++1] (100), 514 (14), 452 (27). Anal. Calcd for $C_{29}H_{39}O_9N$: C, 63.84; H, 7.20; N, 2.57. Found: C, 63.72; H, 7.25; N, 2.50.

Phenyl-4,6-*O*-benzylidene-2,3-dideoxy-β-D-glucopyranosido[2,3-*h*]-*N*-2-methoxyethyl-1,4,7,10-tetraoxa-13-azacyclopentadecane (13). The purification was carried out by column chromatography with eluent CH_2Cl_2:MeOH:NH_4OH = 97:2:1 on silica gel or with eluent CH_2Cl_2:MeOH = 99.2:0.8 on aluminium oxide. Yield: 53.8%; white crystals; M.p.: 57-58 °C (ethanol); $[\alpha]_D$ -40.1° (c 1, $CHCl_3$); IR (KBr, cm^{-1}): 2920, 2876, 1600, 1496, 1388, 1239, 1093, 749, 695; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.70-3.00 (m, 4H, 2 NCH_2 of the macrocycle), 2.75 (t, 2H, *J*=6 Hz, $NCH_2CH_2OCH_3$), 3.33 (s, 3H, $NCH_2CH_2OCH_3$), 3.48 (t, 2H, *J*=6 Hz, $NCH_2CH_2OCH_3$), 3.45-3.84 (m, 12H, H-2, H-3, H-4, H-5 and 4 OCH_2 of the macrocycle), 3.79 (t, 1H, *J*=10.5 Hz, H-6), 3.95-4.15 (m, 4H, 2 OCH_2 of the macrocycle), 4.36 (dd, 1H, *J*=10.5, 5 Hz, H-6), 5.06 (d, 1H, *J*=7.6 Hz, H-1), 5.54 (s, 1H, PhCH), 7.02 (dm, 2H, *J*=7.7 Hz, OPhH-*o*), 7.05 (tm, 1H, *J*=7.2 Hz, OPhH-*p*), 7.30 (tm, 2H, *J*=8.0 Hz, OPhH-*m*), 7.33-7.40 (m, 3H, CHPhH-*m*-*p*), 7.47 (dm, 2H, *J*=7.7 Hz, CHPhH-*o*); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 54.2, 54.3 (2 NCH_2 of the macrocycle), 55.7 ($NCH_2CH_2OCH_3$), 58.8 ($NCH_2CH_2OCH_3$), 66.1 (C-5), 68.7 (C-6), 68.9, 69.0, 70.3, 70.4, 72.3, 72.4 (6 OCH_2 of the macrocycle), 71.0 ($NCH_2CH_2OCH_3$), 81.0, 81.5 (C-3, C-4), 81.7 (C-2), 101.2 (PhCH), 102.2 (C-1), 117.0 (2 OPhC-*o*), 123.0 (OPhC-*p*), 126.0 (2 CHPhC-*o*), 128.2 (2 CHPhC-*m*), 129.0 (CHPhC-*p*), 129.6 (2 OPhC-*m*), 137.3 (CHPhC-*ipso*), 157.1 (OPhC-*ipso*); MS, m/z: 560 [M^++1] (100), 529 (4), 514 (21), 466 (32.). Anal. Calcd for $C_{30}H_{41}O_9N$: C, 64.38; H, 7.38; N, 2.50. Found: C, 64.45; H, 7.31; N, 2.55.

Phenyl-4,6-*O*-benzylidene-2,3-dideoxy-β-D-glucopyranosido[2,3-*h*]-*N*-hydroxypropyl-1,4,7,10-tetraoxa-13-azacyclopentadecane (14). The purification was carried out by column chromatography with eluent CH_2Cl_2:MeOH =

93:7 on silica gel or preperative TLC with eluent CH_2Cl_2:MeOH = 98:2 on aluminium oxide. Yield: 38.4%; light yellow oil; $[\alpha]_D$ -44.9° (c 1, $CHCl_3$); IR (KBr, cm^{-1}): 3120-3600, 2920, 2875, 1600, 1491, 1236, 1093, 756, 692; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.60-1.78 (m, 2H, $NCH_2CH_2CH_2$), 2.60-2.90 (m, 6H, $NCH_2CH_2CH_2$ and 2 NCH_2 of the macrocycle), 3.44-3.85 (m, 15H, $NCH_2CH_2CH_2$, H-2, H-3, H-4, H-5, H-6 and 4 OCH_2 of the macrocycle), 3.93-4.10 (m, 4H, 2 OCH_2 of the macrocycle), 4.35 (dd, 1H, *J*=10.5, 5 Hz, H-6), 4.83 (s, broad, 1H, OH), 5.06 (d, 1H, *J*=7.6 Hz, H-1), 5.54 (s, 1H, PhCH), 7.02 (dm, 2H, *J*=7.7 Hz, OPhH-*o*), 7.05 (tm, 1H, *J*=7.2 Hz, OPhH-*p*), 7.30 (tm, 2H, *J*=8.0 Hz, OPhH-*m*), 7.33-7.40 (m, 3H, CHPhH-*m*-*p*), 7.47 (dm, 2H, *J*=7.7 Hz, CHPhH-*o*); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 28.4 ($NCH_2CH_2CH_2$), 54.3 (2 NCH_2 of the macrocycle), 56.4 ($NCH_2CH_2CH_2$), 64.0 ($NCH_2CH_2CH_2$), 66.1 (C-5), 68.7 (C-6), 68.8, 68.9, 70.2, 70.3, 72.3, 72.5 (6 OCH_2 of the macrocycle), 80.9, 81.4 (C-3, C-4), 81.7 (C-2), 101.2 (PhCH), 102.1 (C-1), 117.0 (2 OPhC-*o*), 123.0 (OPhC-*p*), 126.0 (2 CHPhC-*o*), 128.2 (2 CHPhC-*m*), 129.0 (CHPhC-*p*), 129.6 (2 OPhC-*m*), 137.3 (CHPhC-*ipso*), 157.1 (OPhC-*ipso*); MS, m/z: 560 [M^++1] (100), 542 (3), 514 (4), 466 (30). Anal. Calcd for $C_{30}H_{41}O_9N$: C, 64.38; H, 7.38; N, 2.50. Found: C, 64.41; H, 7.31; N, 2.52.

Phenyl-4,6-*O*-benzylidene-2,3-dideoxy-β-D-glucopyranosido[2,3-*h*]-*N*-3-methoxypropyl-1,4,7,10-tetraoxa-13-azacyclopentadecane (15). The purification was carried out by column chromatography with eluent CH_2Cl_2:MeOH = 95:5 on silica gel or preparative TLC with eluent CH_2Cl_2:MeOH = 99:1 on aluminium oxide. Yield: 66.0%; faint yellow crystals; M.p.: 78 °C (ethanol); $[\alpha]_D$ -44.1° (c 1, $CHCl_3$); IR (KBr, cm^{-1}): 2922, 2876, 1600, 1496, 1388, 1239, 1093, 749, 695; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.72 (m, 2H, $NCH_2CH_2CH_2$), 2.56 (t, 2H, *J*=7.0 Hz, $NCH_2CH_2CH_2$), 2.66-2.88 (m, 4H, 2 NCH_2 of the macrocycle), 3.32 (s, 3H, OCH_3), 3.42 (t, 2H, *J*=6.3 Hz, $NCH_2CH_2CH_2$), 3.45-3.85 (m, 12H, H-2, H-3, H-4, H-5 and 4 OCH_2 of the macrocycle), 3.79 (t, 1H, *J*=10.5 Hz, H-6), 3.95-4.13 (m, 4H, 2 OCH_2 of the macrocycle), 4.36 (dd, 1H, *J*=10.5, 5 Hz, H-6), 5.06 (d, 1H, *J*=7.6 Hz, H-1), 5.54 (s, 1H, PhCH), 7.02 (dm, 2H, *J*=7.7 Hz, OPhH-*o*), 7.05 (tm, 1H, *J*=7.2 Hz, OPhH-*p*), 7.30 (tm, 2H, *J*=8.0 Hz, OPhH-*m*), 7.33-7.40 (m, 3H, CHPhH-*m*-*p*), 7.47 (dm, 2H, *J*=7.7 Hz, CHPhH-*o*); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 27.7 ($NCH_2CH_2CH_2$), 53.2 ($NCH_2CH_2CH_2$), 54.1, 54.2 (2 NCH_2 of the macrocycle), 58.5 (OCH_3), 66.1 (C-5), 68.7 (C-6), 69.2, 69.3, 70.3, 70.4, 72.4, 72.5 (6 OCH_2 of the macrocycle), 70.9 ($NCH_2CH_2CH_2$), 81.0, 81.5 (C-3, C-4), 81.8 (C-2), 101.2 (PhCH), 102.2 (C-1), 117.0 (2 OPhC-*o*), 123.0 (OPhC-*p*), 126.0 (2 CHPhC-*o*), 128.2 (2 CHPhC-*m*), 129.0 (CHPhC-*p*), 129.6 (2 OPhC-*m*), 137.3 (CHPhC-*ipso*), 157.1 (OPhC-*ipso*); MS, m/z: 574 [M^++1] (100), 514 (6), 480 (31). Anal. Calcd for $C_{31}H_{43}O_9N$: C, 64.90; H, 7.55; N, 2.44. Found: C, 64.92; H, 7.61; N, 2.39.

General procedure for the Michael addition was performed as follows: 1.44 mmol of chalcone and 3.36 mmol of 2-nitropropane were dissolved in 3 mL anhydrous toluene, and then 0.1 mmol of crown ether and 0.5 mmol of base were added. The mixture was stirred under argon atmosphere. After completing the reaction (8-45 hours) a mixture of 7 mL of toluene and 10 mL of water was added. The organic phase was processed in the usual manner. The product was purified by preparative TLC or column chromatography on silica gel using hexane-ethyl acetate (10:1) and chloroform as eluent. M.p.: 146-148°C, $[\alpha]_D$ +80.8° (c 1, CH_2Cl_2) for pure (+)-(S) enantiomer;[5] ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.54 (s, 3H, CH_3), 1.63 (s, 3H, CH_3), 3.27 (dd, 1H, *J*=17.2, 3.2 Hz, CH_2), 3.67 (dd, 1H, *J*=17.2, 10.4 Hz, CH_2), 4.15 (dd, 1H, *J*=10.4, 3.2, CH) Hz, 7.18-7.32 (m, 5H, CHPhH), 7.42 (t, 2H, COPhH-*m*), 7.53 (t, 1H, COPhH-*p*), 7.85 (d, 2H, COPhH-*o*).

General procedure for the Darzens condensation: A toluene of 3 mL solution of 1.3 mmol of phenacyl chloride was treated with 1.9 mmol of benzaldehyde and 0.1 mmol of catalyst in 1.0 mL of 30% NaOH solution. The mixture was stirred under argon atmosphere. After completing the reaction 7 mL of toluene were added, the organic phase washed with water, dried over $MgSO_4$ and the solvent evaporated. The product was isolated by preparative TLC or column chromatography using CH_2Cl_2 as eluent. $[\alpha]_D$ -214° (c 1, CH_2Cl_2) for pure 2*R*,3*S* enantiomer;[10] ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 4.08 (d, 1H, *J*=1.9 Hz, CH), 4.29 (d, 1H, *J*=1.9 Hz, CH), 7.35-7.45 (m, 5H, CHPhH), 7.49 (t, 2H, COPhH-*m*), 7.62 (t, 1H, COPhH-*p*), 8.01 (d, 2H, COPhH-*o*).

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