Synthesis of chiral pyridino-15-crown-5 type ligands containing α-D-hexapyranoside unit and their application in asymmetric synthesis

Attila Makó,[a] Péter Bakó,[a]* Áron Szöllősy,[b] Tibor Bakó,[c] Csaba Peltz,[c] and Péter Keglevich[a]

[a]Department of Organic Chemistry and Technology, Budapest University of Technology and Economics, 1521 Budapest, P.O. Box 91, Hungary
[b]Department of General and Analytical Chemistry, 1525 Budapest, P.O. Box 17,Hungary
[c] Spectroscopic Department, EGIS Pharmaceuticals PLC, 1106 Budapest, Keresztúri út 30-38. 1475 Budapest, 10. P.O.Box 100, Hungary
E-mail: pbako@mail.bme.hu

Abstract
The synthesis of novel chiral monoaza-15-crown-5 compounds (**1**-**4**) with pyridine-ring starting from methyl-4,6-*O*-benzylidene-α-*D*-glucopyranoside and methyl-4,6-*O*-benzylidene-α-*D*-mannopyranoside by different methods are reported. These crown ethers showed significant asymmetric induction in a Michael addition (up to 80% ee).

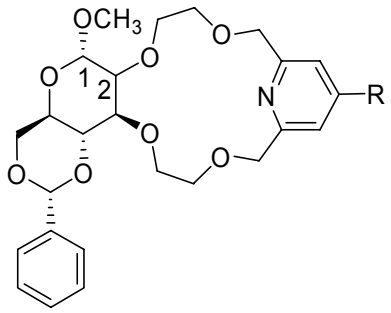
Keywords: Asymmetric catalysis, crown compounds, ring closure, phase-transfer catalysis, Michael addition

Introduction

The application of chiral crown ethers find increasing interest in asymmetric organic synthesis.[1] Crown ethers with carbohydrate moieties form a special group of optically active crown ethers. The inexpensive, natural, non toxic sugars are attractive starting materials for the synthesis of chiral macrocycles. Therefore, these compounds should serv as useful tools for the separation of enantiomers, chiral recognition in enzymatic reactions and for the control of asymmetric reactions.[2] Stoddart *et al.* were the first group that published the enantiomeric discriminating ability of certain sugar-based crown compounds towards the antipodes of chiral ammonium salts.[3] Although many optically active macrocycles incorporating one or more monosaccharide units have been synthesized, only a few have been successfully applied as catalysts in asymmetric reactions.[4] The nature of the crown ether, especially with reference to its chirality, its

rigidity and the micro-environment of its cavity, can all be expected to play a significant role in its functions as a catalyst.

We have previously reported the synthesis of new hexapyranoside-based monoaza 15-crown-5 type lariat ethers with different side-arms containing a heteroatom at the end.[5] These chiral macrocycles proved to be effective asymmetric catalysts in some asymmetric Michael additions,[6] Darzens condensations[6] and epoxidations of double-bond.[7] We focused on the synthesis of the analogue hexapyranoside-based crown ethers incorporating a pyridine unit that were expected to exhibit a more rigid structure. It is known that a more rigid structure is always better from the point of view of enantiomeric discrimination. Mention that it is the Lewis basicity of the pyridine moiety that allows for this discrimination. Besides some of these crown ethers were utilized in the resolution of racemates.[8] We report herein a convenient synthesis of optically active crown ethers **1** – **4** containing two different monosaccharide-units. Changing the substituents on the pyridine ring of the macrocycle **1** can make them suitable for various purposes. For example a methoxy group (**2**) changes the liphophylity of the molecule (that can be phase transfer catalyst) while an allyloxy group (**3**) makes possible the attachment of the ligand to silica gel[9] (Figure 1.).



α-D-Glucopyranoside unit 2C ····· O

1 R = H (40%)

2 R = OCH_3 (29%)

3 R = $OCH_2CH{=}CH_2$ (33%)

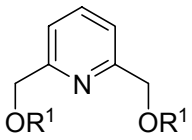
α-D-Mannopyranoside unit 2C ▬ O

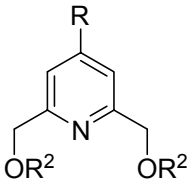
4 R = H (21%)

Figure 1

Results and Discussion

Methods were elaborated in order to synthesize novel chiral monoaza-15-crown-5 compounds (**1-4**) that incorporate pyridine moieties starting from methyl-4,6-*O*-benzylidene-α-*D*-glucopyranoside and methyl-4,6-*O*-benzylidene-α-*D*-mannopyranoside. The key compounds of the syntheses are the 2,6-pyridinedimethyl ditosylates (**6, 9, 14, 16**).[10]





5 R^1 = H (74%)

6 R^1 = Ts (87%)

7 R^1 = CH_2COOCH_3 (72%)

8 R^1 = CH_2CH_2OH (83%)

9 R^1 = CH_2CH_2OTs (80%)

13 R = OMe, R^2 = H (67%)

14 R = OMe, R^2 = Ts (68%)

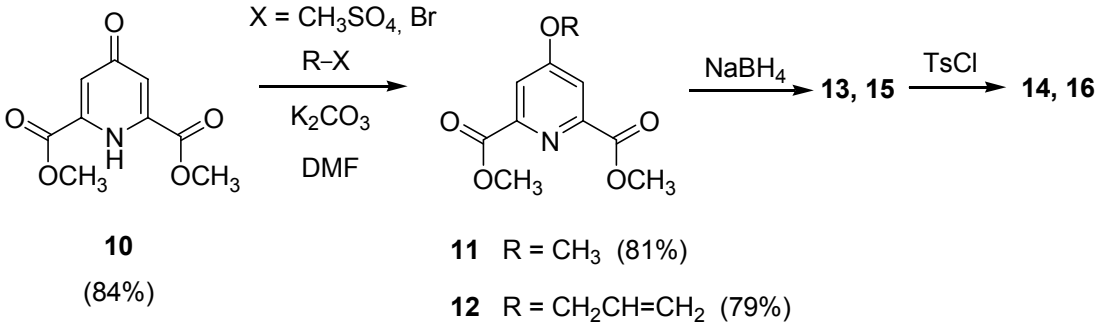
15 R = $OCH_2CH=CH_2$, R^2 = H (62.5%)

16 R = $OCH_2CH=CH_2$, R^2 = Ts (79%)

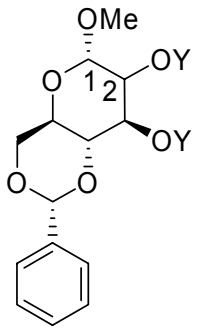
Figure 2

Several possible ways were described for the preparation of 2,6-pyridinedimethyl bistosylate **6**.[11] In our case 2,6-bis(hydroxymethyl)pyridine **5**[12] was treated with p-toluenesulfonyl chloride in a mixture of THF and 40% aqueous NaOH at low temperature[13] to give bistosylate **6** (87% yield). The synthesis of the "half-crown" diol containing a pyridyl unit **8** was accomplished by the reaction of diol **5** with methyl bromoacetate in the presence of sodium hydride in THF under reflux to afford diester **7** (72% yield), which was converted to diol **8** by reduction with $NaBH_4$ in ethanol at ambient temperature (83%).[14] The ditosylate derivative **9** was obtained by the treatment of diol **8** with two equivalents of p-toluenesulfonic chloride in the presence of finely pulverized KOH at low temperature in THF (product **9** was obtained in a 80% yield).[15] Compound **9** was observed to be somewhat unstable (Figure 2).

The dimethyl chelidamate **10** was synthesized by a method described in the literature.[11] Diester **10** was treated with dimethyl sulfate or allyl bromide in DMF, in the presence of K_2CO_3, to obtain 4-substituted dimethyl 2,6-pyridinedicarboxylates **11** and **12,** respectively (see Scheme 1). Diesters **11** and **12** were reduced with $NaBH_4$ in ethanol and the crude ethanol free 2,6-pyridinedimethanol derivatives **13** and **15** so obtained were treated with p-toluenesulfonyl chloride in a mixture of THF and aqueous NaOH at low temperature to give bistosylate **14** and **16,** respectively (Scheme 1).[11]



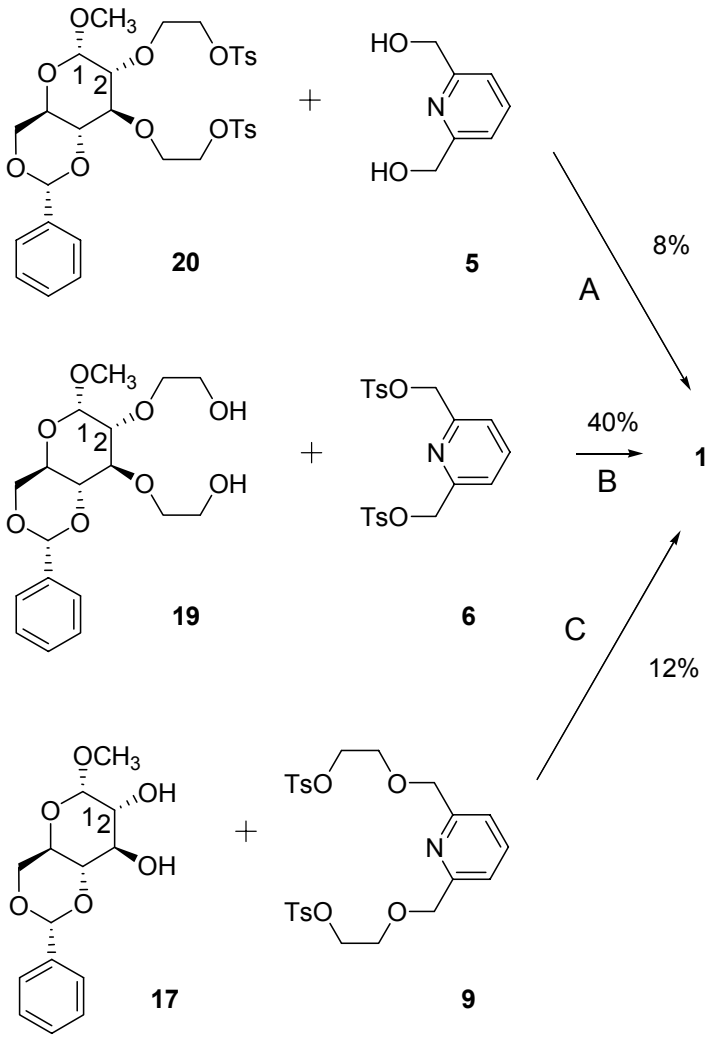
Scheme 1. Synthesis of 4-methoxy- and 4-allyloxy-2,6-pyridinedimethyl ditosylate (**14**,**16**) respectively, R-X means $(CH_3)_2SO_4$ and CH_2=CH-CH_2Br.



	α–D-Glucopyranoside 2C OY	α–D-Mannopyranoside 2C OY
Y = H	**17**	**21**
Y = CH_2COOH	**18** (78 %)	**22** (76 %)
Y = CH_2CH_2OH	**19** (80 %)	**23** (68 %)
Y = CH_2CH_2OTs	**20** (67 %)	

Figure 3

Our chiral compounds were the "half-crown" diol **19** containing a glucopyranoside-unit and its bistosylate derivative **20**, as well as the diol **23** containing a mannopyranoside moiety (Figure 3). The methyl-4,6-O-benzylidene-α-D-glucopyranoside **17** was treated with sodium chloroacetate in DMF in the presence of sodium hydride to give chiral dicarboxylic **18** (78%), which was reduced with a mixture of $NaBH_4$ and I_2 in THF to result in the sugar-based diol **19** in a 80% yield after chromatography. Compound **19** was synthesized earlier in four steps including ozonolysis as described by Stoddart *et al*. (in 51% yield from methyl-4,6-*O*-benzylidene-α-*D*-glucopyranoside).[16] The reaction of diol **19** with p-toluenesulfonyl chloride in THF/aqueous NaOH furnished bistosylate **20** in a yield of 67% after column chromatography. The dicarboxylic with a mannopyranoside-unit **22** and the corresponding diol **23** were obtained from the methyl-4,6-O-benzylidene-α-D-mannopyranoside **21** in a similar way. Compound **23** was prepared earlier from the 2,3-di-O-*tert*-butylester derivative by reduction with $LiAlH_4$ (81% yield for the two steps).[17] As far as we experienced, this method gave **23** in a low yield (50%). The reducing agent $NaBH_4$+I_2 described by Periasamy[18] gave, however, the sugar-based diols **19** and **23** in good yields after column chromatography. Our method possesses some advantages since it avoids the ozonolysis[16] of the diallylderivatives of **17** and reduction[17] with $LiAlH_4$ respectively.



Scheme 2. Preparation of chiral pyridino-crown ether **1** by different methods (reaction conditions: NaH, DMF, 60°C, 40 h).

The synthesis of crown ether **1** was attempted using three different ring closure reactions by varying the coupling partners as shown in Scheme 2. (Methods A, B and C, in DMF in the presence of NaH). The reaction of 2,6-bis(hydroxymethyl)pyridine **5** with glucopyranoside-based diol-ditosylate **20** (Method A) provided macrocycle **1** in only 8% yield. In another version, the reaction of 2,6-pyridinedimethyl ditosylate **6** with **19** glucopyranoside-based diol (Method B) afforded crown ether **1** in 40% yield. The ring forming reaction of ditosylate derivative **9** and sugar derivative **17** (Method C) was not really efficient, as the yield of **1** was only 12%. The yield difference of methods A, B and C may be the consequence of the success of the template effect within both reagents in the intramolecular ring closure reaction. The template effect can be characterized by the complexing abilty of the reagents towards Na^+ cation. The binding power of the reagents was measured in solution (NBA) in the presence of sodium picrate salt by FAB-MS[19-21] to achieve a fast and qualitative screening of the complexation ability of compounds **5**,

6, **9**, **19** and **20**. Table 1 summarizes the relative peak intensities (PI) of [ligand + Na]$^+$ as compared to uncomplexated [ligand + 1]$^+$ that was regarded to be 100%.

Table 1. Sodium binding ability of compounds **5**, **6**, **9**, **19**, **20** on the basis of FAB-MS measurements [a]

	Reagents of ring closure reactions				
Compounds	**5**	**6**	**9**	**19**	**20**
PI = [M+23]$^+$/ [M+H]$^+$	2.8	44	1450	410	900

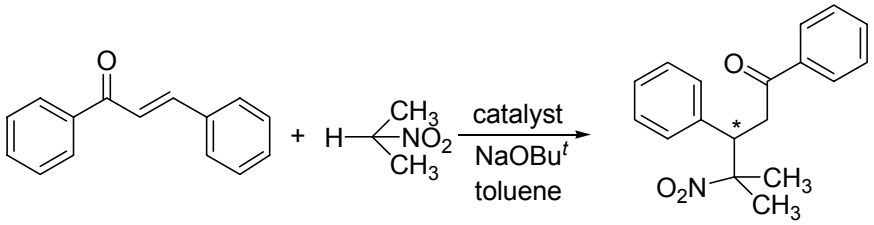
[a]On the basis of relative peak intensities in the presence of sodium picrate salt in NBA matrix, assuming that all ligands form similar 1:1 complex.

As indicated in Table 1 the strong complexing ability of **20** (*PI*=900) and the weak complexing ability of **5** (*PI*=2.8) result in only a low yield in the ring closure reaction. In contrary, the complexing ability of ditosylate **6** is increased (*PI*=44) and the half-crown diol **19** even owes a bigger value (*PI*=410). This is in accordance with the relatively good yield of 40% obtained by Method B. Regarding Method C, the excellent complex forming ability of compound **9** (*PI*=1450) is not enough as the hydroxy groups of sugar derivative **17** are of low reactivity. This situation results in the low yield of 12%. One of our interesting observations is that the incorporation of the tosyl groups results in better coordinating ability for the diols (template effect). For example for **20** created from **19**, the *PI* value is almost doubled (PI_{19} = 410 → PI_{20} = 900). This effect has a special importance in the case of compound **5** that has only a week coordinating ability (PI_5=2.8). Tosylation of **5** results in a 15-fold increase of value *PI* (PI_6=44). This effect has already been observed earlier in respect to crown ethers.[22] It is worth mentioning that beside of the template effect, other circumstance may also play a role in the yield of the ring closure reaction. We have not studied the ability to elimination of tosylates. It is assumed that method B is favored also because compound **6** can undergo only substitution, in contrast to the case of **20** and **9**.

The methoxy- and allyloxy-macrocycles with pyridine ring (**2** and **3**, respectively) were prepared by Method B. The crown ether **2** was prepared by the reaction of pyridine derivative **14** and sugar-based diol component **19** in 29% yield. Similarly, the reaction of **16** and **19** afforded macrocycle **3** in 33% yield. The α-*D*-mannopyranoside-based macrocycle **4** was prepared in an analogue way. The reaction of methyl-4,6-O-α-*D*-mannopyranoside (**21**) with sodium chloroacetate gave bisacid derivative **22,** the reduction of which led to **23** bis-glycol. The reaction of "half crown-diol" **23** and ditosyl derivative **6** resulted in the formation of mannopyranoside-based macrocycle **4** in a yield of 21%. It is noted that compound **4** differs only from **1** in the configuration of its C(2) atom in the sugar moiety. In the glucopyranoside-based **1** the position of the C(2)-O and C(3)-O groups is *trans*, while that is *cis* in **4**. It was observed from the FAB-MS spectroscopy of the crude products that the glucopyranoside-based crown ethers were mainly formed as sodium complexes, while the mannopyranoside-based macrocycle

was present in the crude products in an uncomplexed form. On purification by chromatography on alumina, the complexes were decomposed.

Chiral crown ethers **1-4** were tested in the Michael addition of 2-nitropropane to chalcone (Scheme 3). The solid-liquid phase transfer catalytic reaction was carried out at room temperature in dry toluene, in the presence of solid sodium *tert*-butoxide (35 mol%) and one of the chiral catalysts **1-4** prepared (7 mol%).[6]



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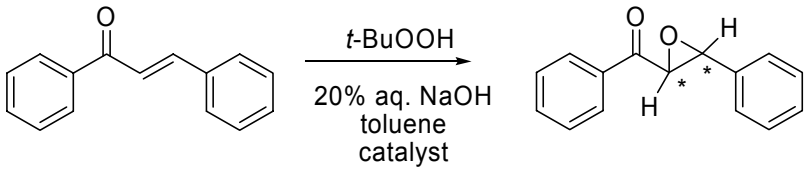
Scheme 3. Asymmetric addition of 2-nitropropane to chalcone.

Table 2. The effect of the crown ether catalysts **1-4** on the enantioselectivity in the addition of 2-nitropropane to chalcone at room temperature

Entry	Catalyst	Time (h)	Yield of **24** (%)[a]	$[\alpha]_D$[b]	ee[c] (%)
1	**1**	24	48	- 58.2	72 (*S*)
2	**2**	30	47	- 61.4	76 (*S*)
3	**3**	30	51	- 54.1	67(*S*)
4	**4**	25	50	+ 64.6	80 (*R*)

[a] Based on isolation by preparative TLC. [b] In CH_2Cl_2 at 20 °C. [c] Determined by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ as chiral shift reagent. Absolute configuration were assigned by comparison of specific rotation with literature value.[6a]

In all cases, the products were isolated by preparative TLC after the usual work-up procedure. The enantiomeric excess (ee) was determined by ^{1}H NMR spectroscopy using (+)-Eu(hfc)$_3$ as a chiral shift reagent. The experimental data are shown in Table 2. It can be seen that glucopyranoside-based macrocycle **1** gave the product **24** in 48% yield and in 72% ee in favour of the *S* enantiomer.[6c] It is also seen that the substituents in the pyridine ring influence the enantioselectivity to only a small extent; in the presence of catalyst **2** (R=OCH_3) and **3** (R=$OCH_2CH{=}CH_2$) the ee was 76 and 67%, respectively. It is interesting, that while the glucopyranoside–based crown ethers (**1-3**) induce the formation of the (-)-(*S*)-enantiomer of the Michael adduct, the mannopyranoside-based species **4** brings about excess of the (+)-(*R*)-enantiomer with ee of 80% .



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Scheme 4. Asymmetric epoxidation of chalcone.

Chiral macrocycles **1-4** were used as catalyst in the epoxidation of *trans* chalcone.[7] In our experiments, the epoxidation of chalcone was carried out with *tert*-butyl hydroperoxide (TBHP, 2 equiv) at 5°C, in toluene, in a liquid-liquid two-phase system, employing 20 % aqueous NaOH (3.5 equiv) as the base and 7 mol % of crown ethers having pyridine-ring **1-4** (Scheme 4). The *trans*-epoxyketone **25** was obtained in all experiments. Table 3 summarizes the results. The epoxidation reaction with these catalysts, however, shows lower enantioselectivity than the Michael addition. The best result of 54% ee was obtained with the glucopyranoside-based catalyst **1** containing no substituent at the pyridine. The lower enantiomer excess (25% and 26% ee) was observed using catalyst **2** and **3** containing methoxy- and allyloxy groups, respectively. It is worth noting that the crown ether incorporating an glucopyranoside unit (**1**-**3**) promoted the formation of the (-)-(2*R*,3*S*) isomer of epoxyketone **25**, while the use of mannopyranoside-based ether **4** resulted in the formation of the other, (+)-(2*S*,3*R*) enantiomer in 47% ee.

Table 3. The effect of the crown ether catalysts **1**-**4** on the enantioselectivity in epoxidation of chalcone at 5°C

Entry	Catalyst	Time (h)	Yield of **25** (%)[a]	$[\alpha]_D$[b]	ee (%)[c]
1	**1**	9,5	38	-115.5	54 (*2R,3S*)
2	**2**	8	36	-53.5	25 (*2R,3S*)
3	**3**	8	40	-55.6	26 (*2R,3S*)
4	**4**	4.5	39	+100.5	47 (*2S,3R*)

[a] Based on isolation by preparative TLC; [b] In CH_2Cl_2 at 20 °C; [c] Determined by ^{1}H NMR spectroscopy in the presence of $Eu(hfc)_3$ as chiral shift reagent. Absolute configuration were assigned by comparison of specific rotation with literature value[7b]

The chiral crown compound synthesised could also be tested in other model reactions as phase transfer catalysts. Currently we are investigating the effect of the crown ethers catalysts in other asymmetric reactions. The allylic substituent in compound **3** makes possible to bind the macrocycle to a solid carrier (silica gel) allowing the separation study of the racemic mixture of chiral ammonium salts.

Experimental Section

General Procedures. All solvents were dried over standard drying agents and freshly distilled. Sodium hydride, used as a mineral oil suspension (60%), was washed with dry hexane prior to use. Melting points were taken on using a Büchi 510 apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer 241 polarimeter at 20°C. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 300 and a Bruker DRX-500 or a Varian Inova 500 instrument in $CDC1_3$ with TMS as the internal standard. Spectral assignment in the ^{1}H NMR and ^{13}C NMR spectra was carried out based on the 2D correlation diagram HSQC, COSY and NOESY. Mass spectra were registrated from m-nitrobenzyl alcohol (NBA) matrix on a Varian MAT 312 instrument. IR spectra were obtained on a Bruker Tensor 37 FT-IR Spectrometer. Elemental analyses were determined on a Perkin-Elmer 240 automatic analyzer. Analytical and preparative thin layer chromatography was performed on silica gel plates (60 GF-254, Merck), while column chromatography was carried out using 70-230 mesh silica gel (Merck). Chemicals and the shift reagent $Eu(hfc)_3$ were purchased from Aldrich Chem. Co.
The known precursors **5-16** were prepared according to literature procedures.[11-15] The structure of the known products was confirmed by comparison of their mp-s, analytical and spectral data (MS, ^{1}H NMR) with those reported in the literature. The yield of the compounds was the following: **5** 74% (Lit.[12] 93%); **6** 87% (Lit.[11] 94%); **7** 72% (Lit.[13] 85%); **8** 83% (Lit.[14] 77%); **9** 80% (Lit.[15] 80%); **10** 84% (Lit.[11] 86%); **11** 81% (Lit.[11] 75%); **12** 79% (Lit.[11] 81%); **13** 67% (Lit.[11] 77%); **14** 68% (Lit.[11] 71%); **15** 62% (Lit.[11] 75%); **16** 79% (Lit.[11] 71%)."

General method for the preparation of compounds 18, 22
A solution of the sugar-derivative **17** or **21** (8.0 g, 28.4 mmol) in dry DMF (50 mL) was added to a well-stirred suspension of NaH (2.88 g 120 mmol) in dry DMF (50 mL). After stirring for 30 min at 60 °C a solution of sodium chloroacetate (13.2 g, 113.6 mmol) in dry DMF (20 mL) was added in small portions. The mixture was heated and stirred at 100 °C for 40 h. After cooling the mixture was treated with water (6 mL). (TLC eluent toluene-MeOH, 2:1.) DMF was removed by distillation in vacuum. The residue was dissolved in $CHCl_3$ and the precipitate was filtered off (sodium salt of the product). The precipitate was dissolved in water (250 mL) and extracted with $CHCl_3$ (3×40 mL). The aqueous phase was cooled to 5 °C and acidified with aq. 20 % HCl to pH 2. The precipitate formed was filtered, dissolved in $CHCl_3$ repeated washed with water, dried (Na_2SO_4) and evaporated to dryness in vacuo to obtain about 11 g of raw product, which was crystallized from a mixture of benzene-acetone.

Methyl-4,6-*O*-benzylidene-2,3-*O*-bis(carboxymethyl)-α-D-glucopyranoside (18). Yield: 8.82 g (78 %) white solid. m.p. 135-136 °C. $[\alpha]_D^{20}$ = +87.9 (c. 1.0, $CHCl_3$). IR (KBr): 3444 (sbr, $\nu_{OH\ COOH}$), 3034-3070 (mw, $\nu_{CH\ Ar}$), 2933 (ms, $\nu_{CH\ alkyl}$), 1738 (ssh, $\nu_{C=O\ COOH}$), 1492 and 1634 (m, $\nu_{CC\ Ar}$), 1455 (m, δ_{CCH} , δ_{OCH}), 1384 (ms, δ_{OCH}), 1217-1317 (mw, ν_{CO}, δ_{CCH}, δ_{COH}), 1198 (mw, δ_{OCH}, δ_{CCH}), 922-1180 (s, ν_{CO}, ν_{CC}), 702 and 755 (msh, γ_{CC}, γ_{CH}) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ:

3.44 (s, 3H, OCH_3), 3.56-3.94 (m, 5H, H-2, H-3, H-4, H-5, H-6), 4.29 (dd, *J* = 4.6, 10.1 Hz, 1H, H-6), 4.27-4.57 (m, 4H, C*H*$_2$COOH), 4.89 (d, *J* = 3.6 Hz, 1H, H-1), 5.51 (s, 1H, C*H*-Ph), 7.37 (t, 2H, PhH-*m*), 7.38 (t, 1H, PhH-*p*), 7,44 (d, 2H, PhH-*o*). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 55.35 (OCH_3), 61.95 (C-5), 68.93, 69.16 (2 *C*H_2COOH), 69.61 (C-6), 79.81 (C-3), 81.27 (C-2), 81.70 (C-4), 98.36 (C-1), 101.66 (*C*H-Ph), 126.03 (2×PhC-o), 128.37 (2×PhC-m), 129.24 (PhC-p), 136.82 (PhC-*ipso*), 175.49 (2×COOH). FAB-MS: 399 $[M + H]^+$, 421 $[M + Na]^+$. HRMS: *m/z* $[M]^+$ calcd for $C_{18}H_{22}O_{10}$: 398.1213 ; found: 398.1218. Anal. Calcd. for $C_{18}H_{22}O_{10}$: C, 54.27 ; H, 5.57 %. Found: C, 54.29; H, 5.60 %.

Methyl-4,6-*O*-benzylidene-2,3-*O*-bis(carboxymethyl)-α-D-mannopyranoside (22). Yield: 8.6 g (76 %). m.p. 146-147 °C. $[\alpha]_D^{20}$ = +10.0 (c. 1.0, $CHCl_3$). IR (KBr): 3448 (sbr, $\nu_{OH\ COOH}$), 3037-3067 (mw, $\nu_{CH\ Ar}$), 2929 (ms, $\nu_{CH\ alkyl}$), 1733 (ssh, $\nu_{C=O\ COOH}$), 1498 and 1635 (m, $\nu_{CC\ Ar}$), 1417 and 1452 (m, δ_{CCH} , δ_{OCH}), 1384 (ms, δ_{OCH}), 1220-1317 (mw, ν_{CO}, δ_{CCH}, δ_{COH}), 1175 (mw, δ_{OCH}, δ_{CCH}), 915-1175 (s, ν_{CO}, ν_{CC}), 701 and 754 (msh, γ_{CC}, γ_{CH}) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.39 (s, 3H, OCH_3), 3.80-4.27 (m, 6H, H-2, H-3, H-4, H-5, 2 x H-6) 4.30-4.39 (m, 4H, C*H*$_2$COOH), 4.78 (d, *J*=1.3 Hz, 1H, H-1), 5.55 (s, 1H, C*H*-Ph), 7.36 (t, 2H, PhH-*m*), 7.38 (t, 1H, PhH-*p*), 7,44 (d, 2H, PhH-*o*). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 55.09 (OCH_3), 63.63 (C-5), 67.55 (*C*H_2COOH), 68.50 (C-6), 69.21, (*C*H_2COOH), 78.69 (C-3), 78.86 (C-4), 79.18 (C-2), 98.72 (C-1), 101.57 (*C*H-Ph), 125.95 (2×PhC-o), 128.38 (2×PhC-m), 129.17 (PhC-p), 137.03 (PhC-*ipso*), 173.62 (2xCOOH), 174.22 (COOH). FAB-MS: 399 $[M + H]^+$, 421 $[M + Na]^+$. HRMS: *m/z* $[M]^+$ calcd for $C_{18}H_{22}O_{10}$: 398.1213; found: 398.1222. Anal. Calcd. for $C_{18}H_{22}O_{10}$: C, 54.27 ; H, 5.57 %. Found: C, 54.39; H, 5.53 %.

General method for the preparation of compounds 19, 23

A solution of the carboxylic acid **18** or **22** (4.0 g, 10 mmol) in THF (10 mL) was slowly added to a suspension of $NaBH_4$ (1.13 g, 30 mmol) in THF (10 mL) at room temperature (10 min). The mixture was stirred until evolution of gas ceases. Iodine (3.18 g, 12.5 mmol) in THF (15 mL) was added slowly (10 min) and additional hydrogen evolved. The contents were further stirred for 5 h. (TLC eluent toluene-MeOH, 10:2.) Dilute HCl (13 mL, 3 N) was added carefully and the mixture was extracted with ether. The combined ether extract was washed with 3 N NaOH (3×25 mL), brine and dried ($MgSO_4$). Evaporation of the organic layer gave the alcohol product, which was purified by column chromatography on silica gel using 2% to 5 % MeOH in $CHCl_3$ as the eluant.

Methyl-4,6-*O*-benzylidene-2,3-*O*-bis(2-hydroxyethyl)-α-*D*-glucopyranoside (19). Yield: 2.96 g (80 %). m.p. 111-114 °C. $[\alpha]_D^{20}$ = +71.8 (c. 1.0, $CHCl_3$). IR (KBr): 3393 and 3499 (sbr, ν_{OH}), 3001-3061 (w, $\nu_{CH\ Ar}$), 2866-2964 (s, $\nu_{CH\ alkyl}$), 1499 and 1667 (m, $\nu_{CC\ Ar}$), 1371-1465 (ms, δ_{OCH}), 1213-1330 (mw, ν_{CO}, δ_{CCH}, δ_{COH}), 905-1194 (s, ν_{CO}, ν_{CC}), 695 and 743 (mssh, γ_{CC}, γ_{CH}) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.43 (s, 3H, OCH_3), 3.51-3.57 (m, 2H, H-2, H-4), 3.68-3.74 (m, 5H, 2 x OCH_2, H-6), 3.80 (dd, *J* = 4.5, 10.0 Hz, 1H, H-5), 3.81- 3.94 (m, 4H, 2 x OCH_2), 4.28 (dd, *J* = 4.5, 10.0 Hz, 1H, H-6), 4.85 (d, *J* = 3.5 Hz, 1H, H-1), 5.54 (s, 1H, C*H*-Ph), 7.36 (t, 2H, PhH-*m*), 7.37 (t, 1H, PhH-*p*), 7,47 (d, 2H, PhH-*o*). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 55.15 (OCH_3),

61.55, 61.70 (2 *C*H_2OH), 62.24 (C-5), 68.85 (C-6), 72.74, 74.34 (2 OCH_2), 77.85 (C-3), 80.18 (C-2), 81.77 (C-4), 98.25 (C-1), 101.38 (*C*H-Ph), 125.90 (2 × PhC-o), 128.18 (2 × PhC-m), 128.99 (PhC-p), 136.95 (PhC-*ipso*). FAB-MS: 371 $[M + H]^+$, 393 $[M + Na]^+$. HRMS: *m/z* $[M]^+$ calcd for $C_{18}H_{26}O_8$: 370.1628; found: 370.1633. Anal. Calcd. for $C_{18}H_{26}O_8$: C, 58.37 ; H, 7.08 %. Found: C, 58.34; H, 7.06 %.

Methyl-4,6-*O*-benzylidene-2,3-*O*-bis(2-hydroxyethyl)-α-*D*-mannopyranoside (23). Yield: 2.52 g (68 %). m.p. 91-92 °C. $[\alpha]_D^{20}$ = +6.4 (c. 1.0, $CHCl_3$). IR (neat): 3421 (sbr, ν_{OH}), 3037-3067 (w, $\nu_{CH\ Ar}$), 2874-2916 (s, $\nu_{CH\ alkyl}$), 1493 and 1639 (m, $\nu_{CC\ Ar}$), 1378-1456 (ms, δ_{OCH}), 1217-1318 (m, ν_{CO}, δ_{CCH}, δ_{COH}), 1200 (mw, δ_{OCH}, δ_{CCH}), 976-1175 (s, ν_{CO}, ν_{CC}), 700 and 756, (mssh, γ_{CC}, γ_{CH}) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.02 (bs, 1H, OH), 3.18 (bs, 1H, OH), 3.39 (s, 3H, OCH_3), 3.63-3.85 (m, 10H, 4 x OCH_2, 2 x CH), 3.87 (d, *J* = 3.7 Hz, 1H, H-3), 3.93-4.08 (m, 2H, 2 x CH), 4.26 (dd, *J* = 4.5, 10.0 Hz, 1H, H-6), 4.74 (d, *J* = 1.3 Hz, 1H, H-1), 5.60 (s, 1H, C*H*-Ph), 7.36 (t, 2H, PhH-*m*), 7.37 (t, 1H, PhH-*p*), 7,46 (d, 2H, PhH-*o*). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 54.90 (OCH_3), 61.23, 61.86 (2 *C*H_2OH), 63.67 (C-5), 68.71 (C-6), 73.43, 73.47 (2 OCH_2 of the podand arm), 76.83 (C-3), 78.21 (C-2), 78.81 (C-4), 100.13 (C-1), 101.75 (*C*H-Ph), 125.97 (2 × PhC-o), 128.24 (2 × PhC-m), 129.04 (PhC-p), 137.16 (PhC-*ipso*). FAB-MS: 371 $[M + H]^+$, 393 $[M + Na]^+$. HRMS: *m/z* $[M]^+$ calcd for $C_{18}H_{26}O_8$: 370.1628; found: 370.1634. Anal. Calcd. for $C_{18}H_{26}O_8$: C, 58,37; H, 7,08 %. Found: C, 58.43; H, 7.05 %.

Methyl-4,6-*O*-benzylidene-2,3-*O*-bis(p-toluenesulphonyloxyethyl)-α-*D*-glucopyrano-side (20). A mixture of diol **19** (2.0 g, 5.4 mmol), NaOH solution (1.0 g, 25 mmol in 8 mL water), THF (8 mL) was stirred for 10 min at RT. The reaction mixture was cooled to 0 °C. A solution of p-toluenesulfonyl chloride (2.17 g, 11.4 mmol) in THF (12 mL) was added dropwise so that the temperature was kept below 5 °C. The reaction mixture was stirred at 0-5 °C for 12 h, then was poured into water (50 mL) and extracted with CH_2Cl_2 (3×50 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo. The product was purified by column chromatography (silica gel; CH_2Cl_2-MeOH, 100:2) furnished **20** as a white solid material. Yield: 2.45 g, (67 %). m.p. 121-122°C. $[\alpha]_D^{20}$ = +28.0 (c. 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.42 and 2,44 (s, 3H, 2×CH_3), 3.35 (dd, *J* = 3.7, 9.3 Hz, 1H, H-2), 3.39 (s, 3H, OCH_3), 3.44 (d, *J* = 9.1 Hz, 1H, H-4), 3.70-4.14 (m, 11H, 4 x CH_2, H-3, H-5 and H-6), 4.26 (dd, *J* = 4.0, 9.4 Hz, 1H, H-6), 4.75 (d, *J* = 3.7 Hz, 1H, H-1), 5.48 (s, 1H, C*H*-Ph), 7.28-7.80 (m, 13H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.50, 21.53 (2xCH_3), 55.25 (OCH_3), 62.02 (C-5), 68.90 (C-6), 69.32, 69.59, 69.98, 70.10 (4 OCH_2 of the podand arm), 79.25 (C-3), 80.19 (C-2), 81.81 (C-4), 98.85 (C-1), 101.18 (*C*H-Ph), 125.91 (2 × PhC-o), 127.78-127.84 (4 x ArC), 128.15 (2 × PhC-m), 128.88 (PhC-p), 129.72-132.97(6 x ArC), 137.12 (PhC-*ipso*), 144.66-144.80 (2 x ArC). FAB-MS: 679 $[M + H]^+$, 701 $[M + Na]^+$. HRMS: *m/z* $[M]^+$ calcd for $C_{32}H_{38}O_{12}S_2$: 678.1805; found: 678.1797. Anal. Calcd. for $C_{32}H_{38}O_{12}S_2$: C, 56.62; H, 5.64 %. Found: C, 56.66; H, 5.65 %.

General method for the preparation of crown ethers 1- 4 (Method B)

A solution of diol **19** or **23** (0.6 g, 1.6 mmol) in dry DMF (10 mL) was added slowly to a well stirred suspension of NaH (0.19 g, 8 mmol) in DMF (10 mL) under Ar and stirred at 60 °C for 30

min. To the mixture, a solution of the appropriate tosylate (**6**, **14** or **16)** (1.6 mmol) in dry DMF (10 mL) was added and the mixture was stirred at 60 °C for further 40 h. After cooling to RT, excess NaH was destroyed by the dropwise addition of water. The solvent was removed, the residue was taken up in the mixture of water (40 mL) and CH_2Cl_2 (40 mL). The aqueous phase was shaken with CH_2Cl_2 (3×40mL). The combined organic phase was dried (Na_2SO_4) and evaporated in vacuum. The crude product was purified by column chromatography on neutral alumina using 1-5 % MeOH in $CHCl_3$ as an eluent to give pure **1**, **2**, **3** and **4** as a solid.

Chiral crown ether 1. Yield: 0.30 g (40 %). m.p. 147-148 °C. $[\alpha]_D^{20}$ = +23.5 (c. 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.45 (s, 3H, OCH_3), 3.53-3.59 (m, 2H, H-2, H-4), 3.63-3.66 (m, 4H, 2 x OCH_2), 3.74-3.85 (m, 3H, H-3, H-5, H-6), 3.87- 4.05 (m, 4H, OCH_2), 4.29 (dd, *J* = 4.6, 10.0 Hz, 1H, H-6), 4.52-4.57 (m, 4H, Ar-CH_2), 4.87 (d, *J* = 3.6 Hz, 1H, H-1), 5.55 (s, 1H, C*H*-Ph), 7.20 (d, *J* = 7.7 Hz, 1H, pyrH-3), 7.27 (d, *J* = 7.6 Hz, 1H, pyrH-5), 7.36 (t, 1H, PhH-*p*), 7,37 (t, 2H, PhH-*m*), 7.49 (d, 1H, PhH-*o*), 7.50 (t, 1H, pyrH-4). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 55.26 (OCH_3), 62.25 (C-5), 69.08 (C-6), 70.07, 70.49, 71.03, 72.42 (4x OCH_2 of the macrocycle), 73.72, 73.85 (Ar-*C*H_2), 78.98 (C-3), 80.18 (C-2), 82.15 (C-4), 98.90 (C-1), 101.28 (*C*H-Ph), 119.44, 119.87 (pyrC-3,5), 126.02 (2 × PhC-o), 126.03 (pyrC-4), 128.21 (2 × PhC-m), 128.91 (PhC-p), 137.40 (PhC-*ipso*), 157.80, 157.81 (pyrC-2,6). FAB-MS: 496 $[M + Na]^+$. HRMS: *m/z* $[M]^+$ calcd for $C_{25}H_{31}NO_8$: 473.2050; found: 473.2053. Anal. Calcd. for $C_{25}H_{31}NO_8$: C, 63.41; H, 6.60 %. Found: C, 63.44; H, 6.58 %.

Chiral crown ether 2. Yield: 0.23 g (29 %). m.p. 142-145 °C. $[\alpha]_D^{20}$ = +26.4 (c. 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.44 (s, 3H, OCH_3), 3.52-3.58 (m, 2H, H-2, H-4), 3.63-3.66 (m, 4H, OCH_2 of the macrocycle), 3.73 (t, *J* = 10.0 Hz, 1H, H-6), 3.79 (s, 3H, pyr-OCH_3), 3.82 (dd, *J* = 4.8, 9.2 Hz, 1H, H-5), 3.84 (t, *J* = 9.2 Hz, 1H, H-3), 3.87-4.03 (m, 4H, OCH_2 of the macrocycle), 4.29 (dd, *J* = 4.7, 10.0 Hz, 1H, H-6), 4.46-4.54 (m, 4H, Ar-CH_2), 4.86 (d, *J* = 3.6 Hz, 1H, H-1), 5.54 (s, 1H, C*H*-Ph), 6.73 (s, 1H, pyrH-3), 6.77 (s, 1H, pyrH-5), 7,35 (t, 2H, PhH-*m*), 7.36 (t, 1H, PhH-*p*), 7.48 (d, 2H, PhH-*o*). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 55.04 (ArO*C*H_3), 55.20 (OCH_3), 62.20 (C-5), 69.04 (C-6), 70.04, 70.42, 71.00, 72.40 (4 OCH_2 of the macrocycle), 73.45, 73.53 (Ar-*C*H_2), 78.87 (C-3), 80.17 (C-2), 82.10 (C-4), 98.82 (C-1), 101.23 (*C*H-Ph), 105.29, 105.61 (pyrC-3,5), 125.98 (2 × PhC-o), 128.17 (2 × PhC-m), 128.86 (PhC-p), 137.35 (PhC-*ipso*), 159.53, 157.60 (pyrC-2,6), 166.93 (pyrC-4). FAB-MS: 526 $[M + Na]^+$. HRMS: *m/z* $[M]^+$ calcd for $C_{26}H_{33}NO_9$: 503.2155; found: 503.2164. Anal. Calcd. for $C_{26}H_{33}NO_9$: C, 62,02; H, 6,61%. Found: C, 62.07; H, 6.57 %.

Chiral crown ether 3. Yield: 0.28 g (33 %). m.p. 129-131 °C $[\alpha]_D^{20}$ = +27.8 (c. 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.44 (s, 3H, OCH_3), 3.52-3.58 (m, 2H, H-2, H-4), 3.63-3.65 (m, 4H, OCH_2 of the macrocycle), 3.73 (t, *J* = 10.1 Hz, 1H, H-6), 3.81 (dd, *J* = 4.6, 9.3 Hz, 1H, H-5), 3.83 (t, *J* = 9.4 Hz, 1H, H-3), 3.85-4.04 (m, 4H, 2xOCH_2 of the macrocycle), 4.28 (dd, *J* = 4.6, 9.9 Hz, 1H, H-6), 4.46, 4.53 (dd, 4H, *J* = 15.0 Hz, Ar-CH_2), 4.49 (d, *J* = 4.7 Hz, 2H, OC*H*$_2$CHCH_2), 4.86 (d, *J* = 3.3 Hz, 1H, H-1), 5.28-5.40 (m, 2H, OCH_2CHC*H*$_2$), 5.54 (s, 1H, C*H*-Ph), 6,00 (m, 1H, OCH_2C*H*CH_2), 6.74 (s, 1H, pyrH), 6.78 (s, 1H, pyrH), 7,35 (t, 2H, PhH-*m*), 7.36 (t, 1H, PhH-*p*), 7.48 (d, 2H, PhH-*o*). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 55.22 (OCH_3), 62.22

(C-5), 68.39 (O*C*H_2CH=CH_2), 69.04 (C-6), 70.05, 70.40, 70.96, 72.43 (4 x OCH_2 of the macrocycle), 73.40, 73.51 (Ar-*C*H_2), 78.85 (C-3), 80.17 (C-2), 82.09 (C-4), 98.80 (C-1), 101.23 (*C*H-Ph), 105.85, 106.12 (pyrC-3,5), 118.18 (OCH_2CH=*C*H_2), 125.99 (2 × PhC-o), 128.17 (2 × PhC-m), 128.87 (PhC-p), 132.27 (OCH_2*C*H=CH_2), 137.36 (PhC-*ipso*), 159.59, 159.68 (pyrC-2,6), 165.91 (pyrC-4). FAB-MS: 552 $[M + Na]^+$. HRMS: *m/z* $[M]^+$ calcd for $C_{28}H_{35}NO_9$: 529.2312; found: 529.2322.

Anal. Calcd. for $C_{28}H_{35}NO_9$: C, 63.50; H, 6.66 %. Found: C, 63.47; H, 6.62 %.

Chiral crown ether 4. Yield: 0.16 g (21 %). m.p. 134-136°C. $[\alpha]_D^{20}$ = + 32.5 (c. 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.35 (s, 3H, OCH_3), 3.62-3.76 (m, 4H, OCH_2 of the macrocycle), 3.78-3.88 (m, 4H, H-2, H-3, H-5, H-6), 3.97-4.07 (m, 4H, OCH_2 of the macrocycle), 4.09 (d, *J* = 9.4 Hz, 1H, H-4), 4.21 (dd, *J* = 4.7, 10.1 Hz, 1H, H-6), 4.57-4.66 (m, 4H, Ar-CH_2), 4.75 (d, *J* = 1.3 Hz, 1H, H-1), 5.59 (s, 1H, C*H*-Ph), 7.17 (d, *J* = 7.7 Hz, 1H, pyrH-3), 7.20 (d, *J* = 7.6 Hz, 1H, pyrH-5), 7.33 (t, 1H, PhH-*p*), 7,35 (t, 2H, PhH-*m*), 7.46 (d, 2H, PhH-*o*), 7.65 (t, 1H, pyrH-4).^{13}C NMR (125 MHz, $CDCl_3$) δ: 54.86 (OCH_3), 63.78 (C-5), 68.85 (C-6), 70.16, 70.68, 71.43, 72.09 (4 x OCH_2 of the macrocycle), 73.13, 74.42 (Ar-*C*H_2), 77.21 (C-3), 78.32 (C-2), 79.54 (C-4), 100.54 (C-1), 101.37 (*C*H-Ph), 122.07, 122.23 (pyrC-3,5), 126.01 (2 × PhC-o), 128.14 (2 × PhC-m), 128.28 (pyrC-4), 128.75 (PhC-p), 137.72 (PhC-*ipso*), 157.49, 158.23 (pyrC-2,6). FAB-MS: 496 $[M + Na]^+$. HRMS: *m/z* $[M]^+$ calcd for $C_{25}H_{31}NO_8$: 473.2050; found: 473.2059. Anal. Calcd. for $C_{25}H_{31}NO_8$: C, 63.41; H, 6.60%. Found: C, 63.52; H, 6.59%.

General procedure for the Michael addition of 2-nitropropane to chalcones[6]

The corresponding azacrown ether catalyst (0.1 mmol) and sodium *tert*-butoxide (0.05 g, 0.5 mmol) was added to a solution of chalcone (0.3 g, 1.44 mmol) and 2-nitropropane (0.3 ml, 3.36 mmol) in dry toluene (3 mL). The mixture was stirred at RT under argon. After a reaction time of 24 to 30 h, a new portion of toluene (7 mL) and water (10 mL) were added and the mixture was stirred for several minutes. The organic phase was washed with water and dried (Na_2SO_4). The crude product obtained after evaporating the solvent was purified by preparative TLC (silica gel, hexane-ethyl acetate, 10:1 as the eluant) to give pure adducts **24.** Yield: 0.21 g (48%). m.p.: 146–148 °C. $[\alpha]_D^{20}$ = -58.2 (c. 1.0, CH_2Cl_2), 72% ee for (-)-(*S*) enantiomer. ^{1}H NMR (500MHz, $CDCl_3$) δ: 7.85 (d, 2H, COPhH-o), 7.53 (t, 1H, COPhH-p), 7.42 (t, 2H, COPhH-m), 7.18–7.32 (m, 5H, CHPhH), 4.15 (dd, *J* = 10.4, 3.3 Hz, 1H, CH), 3.67 (dd, *J* = 17.2, 10.4Hz, 1H, CH_2), 3.27 (dd, *J* = 17.2, 3.2 Hz, 1H, CH_2), 1.63 (s, 3H, CH3), 1.54 (s, 3H, CH_3) ppm. HRMS: *m/z* $[M]^+$ calcd for $C_{18}H_{19}NO_3$: 297.1365; found: 297.1367.

General procedure for the epoxidation of chalcones[7]

A mixture of 0.3 g chalcone (1.44 mmol), the appropriate catalyst (0.1 mmol) in 3 mL toluene and 1 mL 20 % *aq*. NaOH was treated with 0.5 mL 5.5 M *tert*-butyl hydroperoxide in decane (2.88 mmol). The mixture was stirred at 4-5 °C for 4-10 hours. New portion of toluene (7 mL) and water (10 mL) were added and the mixture was stirred for several times. The organic phase was washed with 10% aqueous hydrochloric acid (2 ×10 mL) and then with water (10 mL). The

organic phase was dried (Na_2CO_3). The crude product obtained after evaporating the solvent was purified by preparative *TLC* (silica gel, hexane–ethyl acetate, 10:1 as the eluant) to give **25** in a pure form. Yield: 0.16 g (38%). m.p.: 64-66 ^oC. $[\alpha]_D^{20}$ = –115.5 (c. 1.0, CH_2Cl_2), 54% ee for (2*R*,3*S)* enantiomer; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.02 (d, 2H, COPhH-*o*), 7.63 (t, 1H, COPhH-*p*), 7.50 (t, 2H, COPhH-*m*), 7.38-7.44 (m, 5H, CHPhH) , 4.30 (d, *J* = 1.9 Hz, 1H, CH), 4.09 (d, *J* = 1.9 Hz, 1H, CH). HRMS: *m/z* calcd for $C_{15}H_{12}O_2$ $[M]^+$: 224.0837; found: 224.0830.

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References

1. (a) Kyba, E. P.; Timko, J. M.; Kaplan, L. J.; de Jong, F.; Gokel, G. W.; Cram, D. J. *J. Am. Chem. Soc*., **1978**, *100*, 4555. (b) Cram, D. J.; Sogah, G. D. Y. *J. Am. Chem. Soc.* **1985***, 107,* 8301. (c) O' Donnell, M. I. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; *Asymmetric Phase-Transfer Reactions*; VCH: New York, 2000; pp 727-755. (d) *Comprehensive Asymmetric Catalysis;* Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer: New York, 1999; p 241.
2. Jarosz, S.; Listkowski, A. *Current Org. Chem.* **2006**, *10*, 643.
3. (a) Stoddart, J. F. *Top. Stereochem.* **1987***, 17*, 207. (b) Miethchen, R.; Fehring, V. *Synthesis* **1998***,* 94. (c) Faltin, F.; Fehring, V.; Miethchen, R. *Synthesis* **2002**, 1851.
4. (a) Alonso-Lopez, M.; Jimenez-Barbero, J.; Martin-Lomas, M.; Pemades, S. *Tetrahedron* **1988**, *44*, 1535. (b) Van Maarschalkerwaart, D. A. H.; Willard, N. P.; Pandit, U. K. *Tetrahedron* **1992**, *48*, 8825. (c) Aoki, S.; Sasaki, S.; Koga, K. *Heterocycles* **1992**, *33*, 493. (d) Kanakamma, P. P.; Mani, N. S.; Maitra, U.; Nair, V. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2339. (e) Tőke, L.; Bakó, P.; Keserű, Gy. M.; Albert, M.; Fenichel, L. *Tetrahedron* **1998**, *54*, 213 and references cited therein. (f) Itoh, T.; Shirakami S. *Heterocycles,* **2001***, 55*, 37.
5. Bakó, P.; Tőke, L. *J. Incl. Phenom*. **1995***, 23,* 195.
6. (a) Bakó, P.; Czinege, E.; Bakó, T.; Czugler, M.; Tőke, L. *Tetrahedron:Asymmetry* **1999***, 10*, 4539. (b) Bakó, T.; Bakó, P.; Szöllősy, Á.; Czugler, M.; Keglevich, Gy.; Tőke, L. *Tetrahedron: Asymmetry* **2002***, 13,* 203. (c) Bakó, T.; Bakó, P.; Keglevich, Gy.; Báthori, N.; Czugler, M.; Tatai, J.; Novák, T.; Parlagh, Gy.; Tőke, L. *Tetrahedron:Asymmetry* **2003**, *14*, 1917-1923.
7. (a) Bakó, T.; Bakó, P.; Keglevich, Gy.; Bombicz P.; Kubinyi, M.; Pál, K.; Bodor, S.; Makó, A.; Tőke, L. *Tetrahedron: Asymmetry* **2004**, *15*, 1589. (b) Bakó, P.; Makó, A.; Keglevich,

Gy.; Kubinyi, M.; Pál, K. *Tetrahedron: Asymmetry* **2005**, *16*, 1861.
8. (a) Zhang, X.-X.; Bradshaw, J. S.; Izatt, R. M. *Chem. Rev*. **1997**, *97*, 3313. (b) Samu, E.; Huszthy, P.; Horváth, Gy.; Szöllősy Á.; Neszmélyi, A. *Tetrahedron: Asymmetry* **1999**, *10*, 3615. (c) Köntös, Z.; Huszthy, P.; Bradshaw, J. S.; Izatt, R. M. *Enantiomer* **2000**, 5,561
9. (a) Bradshaw, J. S.; Huszthy, P.; Wang, T.-M.; Zhu, C.-Y.; Nazarenko, A. Z.; Izatt, R. M. *Supramolecular Chem.* **1993**, *1*, 267. (b) Horváth Gy.; Huszthy, P.; Szarvas, Sz.; Szokán, Gy.; Redd, J. T.; Bradshaw, J. S.; Izatt, R. M. *Ind. Eng. Chem. Res*. **2000**, *39*, 3576.
10. (a) Bradshaw, J. S.; Nakatsjui, Y.; Huszthy, P.; Wilson, B. E.; Dalley, N. K.; Izatt, R. M. *J. Heterocycl. Chem.* **1986**, *23*, 353.
11. Horváth, Gy.; Rusa, C.; Köntös, Z.; Gerencsér, J.; Huszthy, P. *Synth. Commun.* **1999**, *29*, 3719, and referenced herein.
12. Newcomb, M.; Timko, J. M.; Walba, D. M.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6392.
13. Cabezon, B.; Cao, J.; Raymo, F. M.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **2000**, *6*, 2262.
14. Bell, T. W.; Cheng, P. G.; Newcomb, M.; Cram, D. J. *J. Am. Chem. Soc*. **1982**, *104*, 5185.
15. Marchand, A. P.; Chong, H.-S.; Takhi, M.; Power, T. D. *Tetrahedron*, **2000**, *56*, 3121.
16. Dale, J.; Laidler, A.; Stoddart J. F. *Carbohydr. Res.,* **1977**, *55*, 1.
17. Pietraszkiewicz, M; Juczak, J. *Tetrahedron*, **1984**, *40*, 2967.
18. Kanth, J. V. B.; Periasamy, M. *J. Org. Chem*. **1991**, *56*, 5964.
19. Johnstone, R. A.; Lewis, I. A. S.; Rose, M. E. *Tetrahedron*, **1983**, *39*,1597.
20. Stibor, I.; Holy, P.; Závada, J.; Koudelka, J.; Novák, J.; Zajicek, J.; Belohradsky, M. *J. Chem. Soc. Chem. Commun.* **1990**, 1581.
21. Tsukube, H.; Inoue, T.; Hori, K. *J. Org. Chem*. **1994**, *59*, 8047.
22. Bakó, P.; Fenichel, L.; Tőke, L.; Czugler, M. *Liebigs Ann. Chem.* **1981**, 1163.