Tetrahedron Vol. 48, No. 40, pp. 8825-8840, 1992
Printed in Great Britain

0040-4020/92 $5.00+.00

Synthesis of Carbohydrate containing Crown Ethers and their application as Catalysts in Asymmetric Michael Additions

Dave A.H. van Maarschalkerwaart, Nico P. Willard and Upendra K. Pandit*

Laboratory of Organic Chemistry, University of Amsterdam,
Nieuwe Achtergracht 129, 1018 WS Amsterdam. The Netherlands.

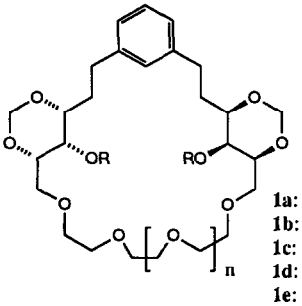
(*Received in UK* 29 *July* 1992)

Key Words : chiral crown ethers; carbohydrates; asymmetric catalysis; asymmetric Michael additions

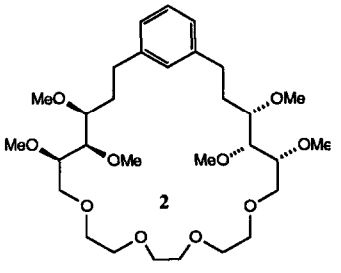
Abstract: *Synthesis of carbohydrate containing crown ethers tuned with steric and micro-environmental features and their application as catalysts in the Michael addition of methyl phenylacetate to methyl acrylate to give a chiral product is reported. The mechanistic rationale of the asymmetric induction is discussed.*

INTRODUCTION

Catalytic asymmetric C-C bond formation reactions are of special interest in organic synthesis[1]. The mechanism leading to asymmetric induction in transition states in the case of asymmetric reactions catalyzed by chiral crown ether complexes is not well understood. Many optically active crown ethers have been synthesized[2], of which only a few have been applied as catalysts in asymmetric reactions[3a-f]. The nature of the crown ether, especially with reference to its chirality, its absolute stereochemistry, its rigidity and the micro-environment of its cavity, can all be expected to play an important role in its function as a catalyst.



1a: n=1, R=H
1b: n=1, R=CH_2Ph
1c: n=2, R=CH_2Ph
1d: n=1, R=Me
1e: n=2, R=Me
1f: n=2, R=H



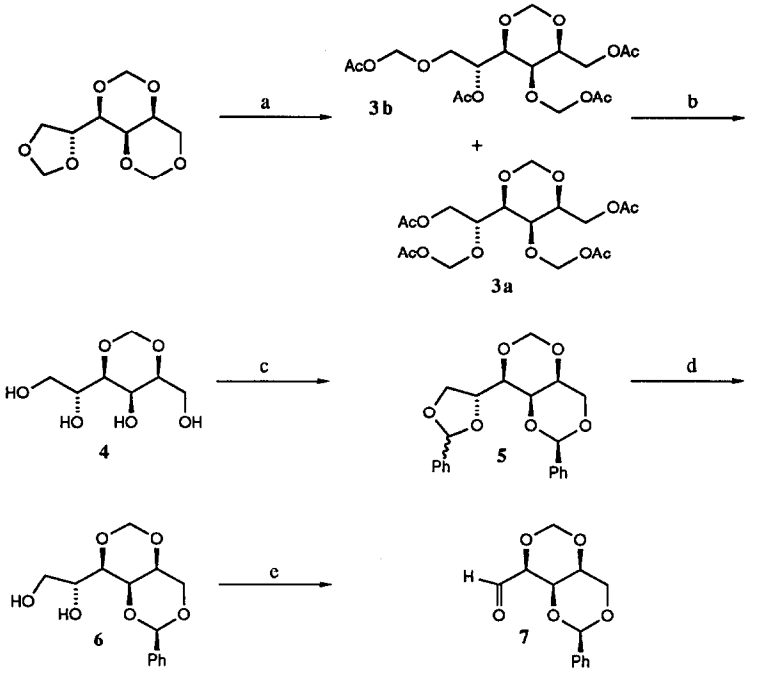
As a part of a program directed to the study of (co)enzyme-like catalysts and reagents[4], we have prepared a class of chiral crown ethers which possess cavities with varying steric characteristics and hydrophobic and polar regions and have examined their potential as catalysts in a chiral C-C bond formation reaction. For the introduction of chirality in the crown ethers, the use of carbohydrates with their rich array of stereogenic centres, and tunable rigidity and, last but not the least, their availability, appeared a highly attractive choice. This has also been recently recognized by other workers in the field[3c,d,f]. In the

context of the present investigation, we considered it highly relevant to introduce steric factors and regions of different polarity in the cavity of the macrocyclic ring system. With these objectives in mind, the crown ethers **1a-f** and **2** were synthesized.

Several special features of the abovementioned macrocyclic compounds may be pointed out. These crown ethers are characterized by a C_2 axis of symmetry. They all possess, besides the chiral carbohydrate moieties, two distinctly separate regions of micro environment; namely, an aromatic hydrophobic region containing the phenyl group, and a polar region consisting of the polyethylene ether chain. The configurations of the asymmetric carbons in **1a-f** (derived from L-xylose) are opposite to those in **2** (derived from D-xylose). Inspection of CPK models reveals that in **1b-c**, the benzyl ether substituents are situated as pendent groups above (β) and below (α) the mean plane of the macrocycle and that they consequently sterically block the hydrophobic region in the vicinity of the aromatic moiety. In addition, the *cyclic* acetals of the 1,3-diol system, confer a rigid conformation to the macrocyclic frame-work. In comparison, the macroring of compound **2** possesses a more flexible character, due to protection of the same 1,3-diols as *acyclic* methyl ethers, furthermore, its hydrophobic region is free from steric obstruction to approach of reactants due to absence of the bulky benzyl substituents. The implications of these structural considerations in the catalysis mediated by **1a-e** and **2** will be discussed in the sequel.

SYNTHESIS

The cyclic acetal compounds



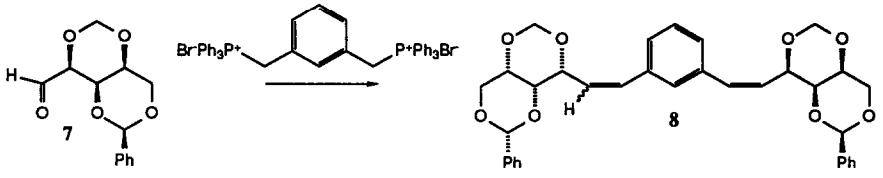
(a) Ac_2O, HOAc, H_2SO_4; 95 % (b) Na, MeOH, CH_2Cl_2; 91 % (c) PhCHO, H^+, DMF/cyclohexane; 75 % (d) HCO_2H, $ClCH_2CH_2Cl$/EtOH; 69 % (e) $NaIO_4$, dioxane; 83 %.

Scheme 1

As described above the new crown ether compounds consist of different parts. The hydrophobic region (the "northern fragment") consists of a m-xylyl derivative which is responsible for sufficient rigidity in the molecule. The "eastern and western" fragments possess the chirality. The hydrophobic region (the "southern fragment") is built of polyethylene derivatives and due to the lone pair electrons of the oxygens the complexation would be expected to take place in this region. Via a double Wittig reaction[5] with a suitable aldehydo carbohydrate the m-xylyl moiety is attached to the chirality bearing synthons. As chiral synthons we used derivatives of D- and L-xylose, which also have been succesfully applied in the total synthesis of Sesbanimide A[6a] and several derivatives[6b].

Acetolysis of tri-*O*-methylene-D-glucitol[7] led nearly quantitatively to a mixture which consists of the regioisomeric tetraacetates **3a** and **3b** in a 15:1 ratio (Scheme 1). In seperate batches different ratios were observed. Transesterfication of the ester functionalities with a catalytic amount of sodium in methanol and dichloromethane resulted in tetraol **4**. In order to have access to the 1,2-dihydroxyl moiety selectively, which is vulnerable to oxidative cleavage, the tetraol **4** was first treated with a solution of benzaldehyde in a DMF/cyclohexane mixture in the presence of a catalytic amount of sulphuric acid. Removal of the water with a Dean-Stark apparatus furnished the dibenzylidene derivative **5** as a mixture of epimers on the new stereogenic carbon atom in the dioxolane moiety, in a 9:1 ratio. It is known that dioxolane benzylidene acetals can be hydrolyzed selectively in the presence of dioxane benzylidene acetals[8]. Unfortunately, in the case of compound **5** this proved difficult. The tunability of the reaction was disappointing. The best result was a 69 % yield of diol **6**, but due to the sensitivity of the dioxane moiety sometimes the product was contaminated with tetraol **4**. Several attempts to improve the yield and reproducibility via selective hydrogenolysis were not satisfactory. Oxidation of diol **6** with sodium periodate led to the formation of aldehyde **7** in 83 % yield.

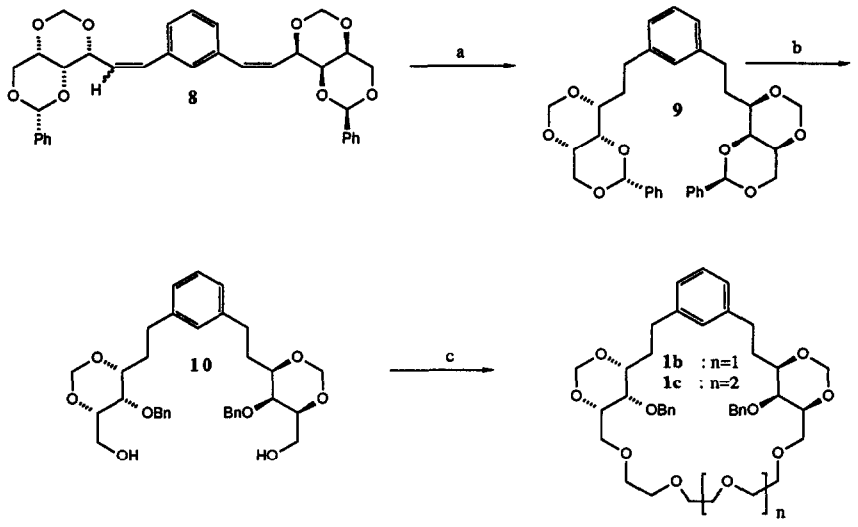
Table 1. Wittig Reaction.



base	temp	yield	solvent	Z,Z : Z.E
LDA	-20°C	48 (%)	THF	2 : 1
BuLi	rt	65 (%)	THF	1 : 3
K_2CO_3	rt	72 (%)	DMF	>10 : 1
K_2CO_3	rt	46 (%)	MeCN	3 : 1
KOtBu	rt	10 (%)	DMF	>10 : 1

The Wittig reaction[5] is accomplished through the bisylid intermediate. At room temperature the reaction furnished the condensation product **8** as a mixture of Z,E- en Z,Z-isomers (E,E-isomer is not detected) in a 65 % yield (Table 1). On a small scale the reaction with butyl lithium in THF and with potassium carbonate in DMF lead to the product **8** in a comparable yield. On a larger scale (24 mmol aldehyde) the butyl lithium/THF version afforded better reproducible results, in addition the reaction work-up was less laborious. As is shown in Table 1 the formation of the Z,E- and Z,Z-isomers depends on the base/solvent combination used. It is observed that there is a clear preferation for Z-stereochemistry at the newly formed C-C bond and that salt free conditions stimulate the formation of Z-stereoisomers. The composition of this mixture is not important to the synthetic strategy, because the benzylic double bonds are

hydrogenated in the following step to give the saturated compound **9** (Scheme 2).



(a) H_2, 10 % Pd/C, CH_2Cl_2; 82 % (b) $LiAlH_4/AlCl_3$, Et_2O/CH_2Cl_2; 67 % (c) NaH, $TsOCH_2CH_2OCH_2[CH_2OCH_2]_nCH_2OTs$, THF; 43 % (n=1), 20 % (n=2).

Scheme 2

Upon treatment with the $LiAlH_4/AlCl_3$ reagent[9] the benzylidene acetals are transformed reductively to the primary diol **10** in regioselective manner, in a yield of 67 % (Scheme 2). This diol is suitable for macrocyclization with the appropriate ditosylated ethyleneglycol derivatives (Scheme 2).

Table 2. Macrocyclization reactions

base (eq.)	temp.	yield	solvent	n	compound
KOtBu (2.5)	reflux	12 (%)	THF	1	**1b**
KOtBu (2.1)	rt	0 (%)	DMF	1	**1b**
NaH (2.4)	reflux	43 (%)	THF	1	**1b**
KH (2.5)	reflux	39 (%)	THF	1	**1b**
NaH (3.0)	reflux	21 (%)	THF	2	**1c**
KH (2.5)	reflux	18 (%)	THF	2	**1c**

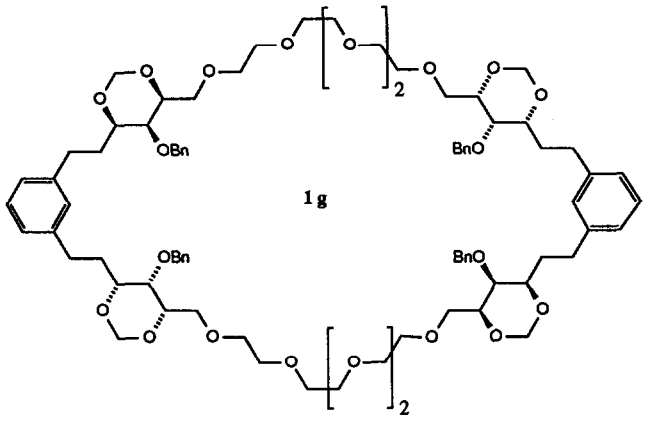
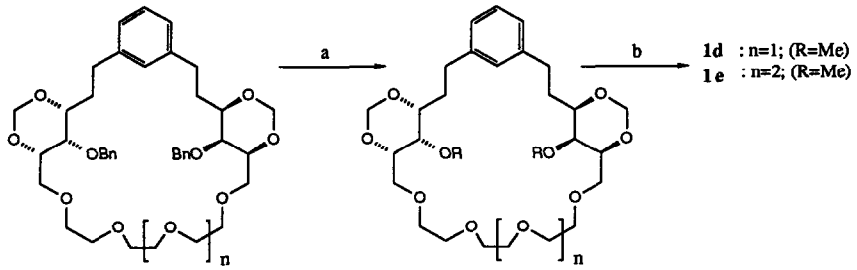


Figure 1

The macocyclizations were carried out using various bases (Table 2).The best macrocyclization results are obtained with NaH as base in refluxing THF. The yields decline as the ring size increases. In the case of n=2 a product, we assume to be the [2+2] dimer **1g**, was isolated in 23 % yield (Figure 1). Due to the same symmetry as in **1c**, the ^{13}C-and the ^{1}H-NMR spectra of **1g** are identically to those of the monomer **1c**, however **1g** is distinctly different since it is much more polar.



1b : n=1
1c : n=2

1a : n=1; (R=H)
1f : n=2; (R=H)

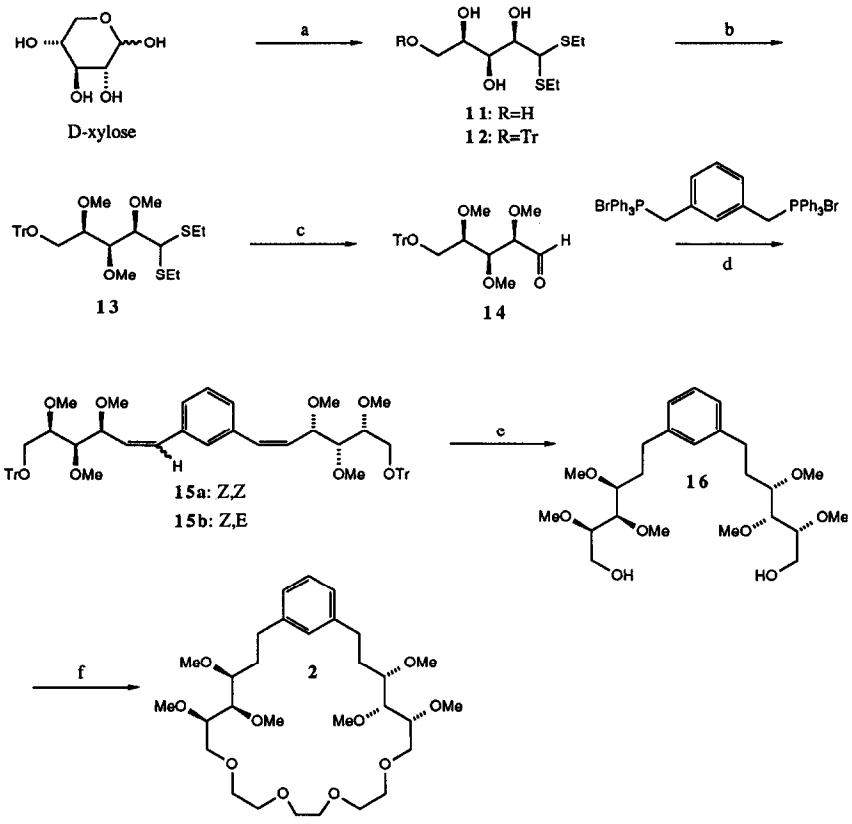
(a) H_2, 10 % Pd/C, EtOH; 99 % (n=1), 74 % (n=2). (b) MeI, NaH, DMF; 90 % (n=1), 100 % (n=2).

Scheme 3

Hydrogenolysis of the benzylethers of **1b** and **1c** led to the diols **1a** and **1f** and subsequent alkylation with MeI provided the dimethoxy derivatives **1d** and **1e** in high yields (Scheme 3).

The acyclic methyl ether compound

The synthetic approach to the crown ether with acyclic methyl ethers **2** is conceptually the same as that employed in the case of the crown ethers with the cyclic methylene acetals. D-xylose is converted into its dithioacetal[10] **11** (Scheme 4). Tritylation of the primary hydroxyl afforded the partial protected derivative **12**. Methylation of the secondary hydroxyl groups gave the fully protected xylose derivative **13**. Cleavage of the thioacetal function was accomplished following the Corey procedure[11] to yield aldehyde **14**.



(a) (1) EtSH, conc. HCl; (2) TrCl, EtN, DMAP, CH_2Cl_2; 84 % (b) NaH, MeI, DMF; 99 % (c) $HgCl_2$, HgO, MeCN, H_2O; 85 % (d) BuLi, THF (e) H_2 55 psi, 10 % Pd/C, EtOH/ 1M HCl (9/1); 40 % (from 14) (f) NaH, $TsOCH_2CH_2OCH_2CH_2O$ CH_2CH_2OTs, THF; 46 %.

Scheme 4

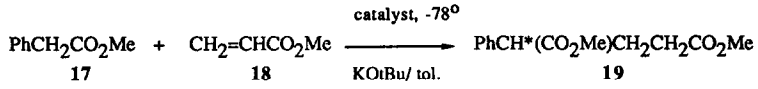
Treatment of the aldehyde **14** under the previously mentioned Wittig reaction conditions resulted in a mixture which, probably consisted of unseparable mixture of the Z,E- and Z,Z-isomers **15a** and **15b**. This mixture was hydrogenated under high pressure in ethanol containing 1M hydrochloric acid. Under these conditions the diol **16** was obtained in 40 % yield (from the aldehyde **14**). The latter was subsequently cyclized to the macrocyclic product **2** in 46 % yield.

MICHAEL ADDITION REACTION RESULTS

The model reaction selected for testing the catalytic activity of the macrocycles was the Michael addition of methyl phenylacetate (**17**) to methyl acrylate (**18**), in the presence of catalytic quantities of the macrocycle, employing potassium tertiary butoxide as a base[3a]. The reactions were carried out at -78° C in toluene. The reagents were used in the following ratios: methyl phenylacetate : methyl acrylate : potassium tertiary butoxide : macrocycle as 2 : 1 : 0.05 : 0.05. The asymmetric induction, expressed in terms of the enantiomeric excess (ee), was monitored by measuring the optical rotation of the product ester (**19**). The

results of the experiments are presented in Table 3.

Table 3. Michael addition reactions



Reaction of 17 (2 eq.) with 18 (1 eq.) in the presence of catalyst (0.05 eq.) and KOtBu (0.05 eq.)

catalyst	time	yield of 19	$[\alpha]_D^{EtOH,rT}$	ee (%)
1a	3 hrs	16 (%)	+ 1.4°	< 2 (S)
1b	1 hr	92 (%)	+ 0.55°	< 2 (S)
1c	1 hr	90 (%)	+ 51.6°	58 (S)
1d	4 hrs	---	---	---
1e	4 hrs	---	---	---
2	1 hr	83 (%)	+ 47.0°	53 (S)
18-crown-6	3 hrs	77 (%)	---	---
no catalyst	2 hrs	30 (%)	---	---

From the results presented in Table 3, several salient aspects of the reaction may be noted. Firstly, except for **1a**, **1d** and **1e**, the chiral crown ethers catalyze the reaction with a high turnover number. Secondly, it is highly significant that the catalysts derived from both L-xylose (**1c**) and D-xylose (**2**) cause asymmetric induction leading to the product with the same (**S**) configuration. Thirdly, the macrocycle in which the ring is enlarged in the polar (polyethylene ether) region of the molecule (**1c**) is more effective as a chiral catalyst than the corresponding smaller ring system (**1b**). Finally, it is recognized that while the degree of chiral induction achieved in these experiments is modest, it is comparable to the results reported by other workers[3c-d], who have employed crown ethers incorporating carbohydrates.

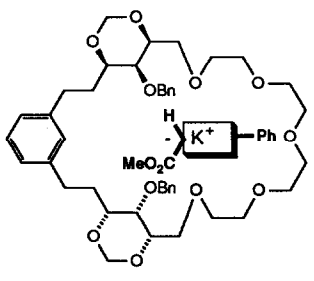


Figure 2

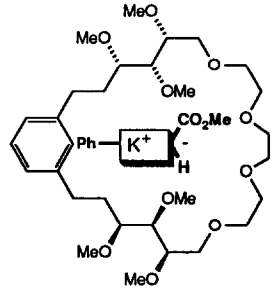


Figure 3

In considering the mechanism of catalysis, it may be expected that the potassium ion of the base (KOt-butoxide) shall coordinate with the ether oxygens within the polar cavity of the macrocycle. The nucleophile derived from phenylacetate (**17**) will bind to this potassium (ionically), and assume a conformation relative to the catalyst which will be determined by both the steric effects of the pendant substituents and the micro-environment of the ring-enclosure. This conformational alignment in the transition state will determine the configuration of the newly generated chiral carbon in the C-C bond-

formation process of the Michael addition reaction.

When the anion of **17** is brought in close proximation to the β-face of the polyethylene polar region of catalyst **1c** (Figure 2), the most favourable orientation is achieved when (a) the phenyl group of **17** is diverted away from the aromatic moiety of the macrocycle, due to steric interactions with the β-benzyl group, and (b) the ester substituent is located in the least hindered position; that is, towards the α-benzyl moiety. In contrast to this, the β-face of **2** is free from steric hindrance and consequently, the alignment of the anion of **17** will be expected to be controlled by the micro-environmental region of the catalyst. This should result in locating the phenyl substituent in the hydrophobic region (β-face) and aligning the ester group above the α-methyl ethers (Figure 3). The transition states of the reactions of the catalyst-anion complexes (Figures 2 and 3) with acrylic ester (**18**), should result in the formation of product **19** with the S configuration, as is indeed observed experimentally.

In the reactions in which the macrocycles, containg the cyclic methylene acetal groups and the methylated secondary hydroxyl functions namely **1d** and **1e** are employed as catalysts no product was obtained. The reason for this is not clear. The reaction in the presence of crown ether **1a**, does not involve the coordinated potassium but the metal salt of one of the free hydroxyl groups. The alkoxide ion system of the macrocycle is presumably sterically too crowded to function as a basic catalyst. Consequently, both the yield of the adduct and the chiral induction are rather poor. In case of catalyst **1b**, the high turnover number coupled with the low chiral induction, deserves comment. In comparison with the analogous but more flexible ring of **1c**, the shorter ring of the catalyst **1b** severely hinders the facile association with the substrate (**17**-anion). Such hindrance would result in the fact that the catalyzed Michael addition reaction occurs largely outside the chiral environment of the crown ether catalyst. The high yields of **19** are similar to the result observed for the same reaction in the presence of 18-crown-6 where, owing to coordination of the K^+-ion (with the catalyst), the complexation presumably increases the nucleophilic character of the ester (**17**) anion. In this context it should be noted that in the absence of a crown ether catalyst a low yield of the Michael adduct is obtained[3d].

In conclusion, it is suggested that the chiral induction in C-C bond formation reactions by crown ether catalysts can be influenced in a predictable manner by the introduction of micro- environmental as well as steric factors. The tuning of crown ethers for the catalysis of chiral induction of centres with a *desired* configuration is a subject of continued interest.

EXPERIMENTAL

General information: Infrared (IR)-spectra are recorded on a Perkin Elmer 298 and are reported in cm^{-1}. Proton nuclear resonance (^{1}H-NMR) spectra are recorded on a Bruker AC 200 or WM 250- or an AMX 300-spectrometer. The Brucker instruments are also used for recording carbon nuclear magnetic resonance (^{13}C-NMR) spectra (50, 62.9, 75.5 MHz, respectively). The chemical shifts are given in ppm downfield of tetramethylsilane. Coupling constants (J) are given in Hertz (Hz). As is indicated shift correlation spectroscopy (COSY), attached proton test (APT), distortionless enhancement by polarization transfer (DEPT), double resonance and ^{1}H-^{13}C correlation experiments are occasionally used for signal assignments. The mass spectra are obtained on a Varian-MAT 711 or on a V.G. Micromass ZAB-HFqQ massspectrometer coupled to a V.G. 11/250 data system. Ionization techniques are given as EI (Electron Impact; 70 eV ionization energy used), and FAB (Fast Atom Bombardment). Accurate mass measuremens are performed on a Varian Mat 711. Thin layer chromatography (TLC) is performed using silicagel coated plastic sheets (Merck silicagel 60 F_{254}) and UV and/or iodine and/or anisaldehyde/H_2SO_4 reagent and/or MeOH/H_2SO_4 reagent for detection. Optical rotations are measured on a Perkin Elmer 241 polarimeter. Chromatographic purification refers to flash chromatography using Merck silicagel 60 (230-400). Microanalyses are carried out at the Chemical Laboratories of the Rijksuniversiteit Groningen. Melting points are determined on a Leitz melting point microscope and are uncorrected. When necessary, reactions are performed in oven dried (overnight 140° C) glassware under a nitrogen atmosphere in absolute solvents. Reagents are purified before use when appropriate.

3,5-Di-*O*-acetoxymethyl-1,6-di-*O*-acetyl-2,4-*O*-methylene-D-glucitol 3a and 3,6-di-*O*-acetoxymethyl-1,5-di-*O*-acetyl-2,4-*O*-methylene-D-glucitol 3b.

To a cooled (icebath) mixture of 370 mL (401 g, 3.9 mol) Ac_2O, 160 mL HOAc, 5 mL H_2SO_4 is added 172.49 g (0.79 mol) of powdered tri-*O*-methylene-D-glucitol[7]. The suspension is stirred vigorously and will become a solution after a while. After stirring for two hours at ± 0° C the temperature is allowed to increase to ± 10° C. Then the transparant solution is poured into 2-3 L icewater and this mixture is stirred for another two hours (mechanical stirrer). The white suspension is extracted with dichloromethane. The organic layers are combined and concentrated *in vacuo*. The two remaining aqueous layers are stirred each overnight with 200 mL dichloromethane. Extraction and then combining the organic layers with the residue of the first extraction and partial concentration *in vacuo* and washing with 2x 100 mL H_2O and 2x 100 mL of a saturated $NaHCO_3$ solution yielded after drying ($MgSO_4$) and concentration *in vacuo* a white solid which consists of a mixture of regioisomers **3a** and **3b** (± 15:1). Yield 318.16 g (0.75 mol, 95 %). 3,5-di-*O*-acetoxymethyl-1,6-di-*O*-acetyl-2,4-*O*-methylene-D-glucitol **3a**: **IR** ($CHCl_3$) 3020, 3000, 2950, 2865, 2770, 2760 cm^{-1}. **^{1}H-NMR** (C_6D_6, 250 MHz): δ 5.49 (d, J = 6.1 Hz, 1H, OCH_2OAc), 5.44 (d, J = 6.4 Hz, 1H, OCH_2OAc), 5.15 (d, J = 6.1 Hz, 1H, OCH_2OAc), 5.01 (d, J = 6.4 Hz, 1H, OCH_2OAc), 4.88 (d, J = 6.1 Hz, 1H, OCH_2O), 4.69 (dd, J = 12.6 + 2.3 Hz, 1H, 6b), 4.42 (dd, J = 11.5 + 7.6 Hz, 1H, 1b), 4.31 (m, 1H, OCH_2O), 4.28 (dd, J = 11.5 + 4.7 Hz, 1H, 1a), 4.10 (dd, J = 12.6 + 3.7 Hz, 1H, 6a), 3.89 (ddd, J = 8.9 + 3.7 + 2.3 Hz, 1H, 5), 3.59 (m, 1H, 3), 3.43 (m, 1H, 4), 3.39 (ddd, J = 7.6 + 4.7 + 1.4 Hz, 1H, 2). 3,6-di-*O*-acetoxymethyl-1,5-di-*O*-acetyl-2,4-*O*-methylene-D-glucitol **3b**: **IR** ($CHCl_3$) 3020, 3010, 2950, 2860, 2770, 1745 cm^{-1}. **^{1}H-NMR** (C_6D_6, 250 MHz): δ 5.25 (d, J = 6.4 Hz, 1H, OCH_2OAc), 5.18 (ddd, J = 7.8 + 4.3 + 2.1 Hz, 1H, 5), 5.06 (d, J = 6.1 Hz, 1H, OCH_2OAc), 5.05 (d, J = 6.1 Hz, 1H, OCH_2O), 5.02 (d, J = 6.4 Hz, 1H, OCH_2OAc), 4.93 (d, J = 6.1 Hz, 1H, OCH_2OAc), 4.31 (d, J = 6.1 Hz, 1H, OCH_2O), 4.28 (d, J = 11.4 Hz, 1H, 1b), 4.11 (dd, J = 11.2 + 2.1 Hz, 1H, 6b), 4.08 (dd, J = 11.4 + 5.3 Hz, 1H, 1a), 3.89 (dd, J = 11.2 + 4.3 Hz, 1H, 6a), 3.73 (dd, J = 7.8 + 1.4 Hz, 1H, 4), 3.59 (bs, 1H, 3), 3.41 (dt, J = 5.3 + 1.6 Hz, 1H, 2). Mixture of **3a**:**3b**(=1:2): **^{13}C-NMR** ($CDCl_3$, 50 MHz; assignment with APT) : δ 170.6 + 170.5 + 170.4 + 170.3 + 170.3 + 170.1 + 170.0 + 170.0 (CO), 93.4 + 89.7 (OCH_2O), 88.8 + 86.8 (OCH_2OAc), 76.6 + 76.4 + 73.9 + 72.1 (2 + 3 + 4 + 5 (**3a**)), 76.3 + 76.1 + 72.0 + 70.4 (2 + 3 + 4 + 5 (**3b**)), 66.8 + 63.4 (1 + 6 (**3a**)), 63.8 + 60.9 (1 + 6 (**3a**)), 20.9 + 20.8 + 20.7 + 20.7 + 20.6 (CH_3CO_2). **Microanalysis**: C calcd. 48.34 %, obs. 47.72 %, H calcd. 6.16 %, obs. 6.23 % (1.5 % H_2O). **mp**: 76 - 78° C.

2,4-*O*-Methylene-D-glucitol 4.

318.16 g (0.75 mol) Of the mixture tetraacetates **3a** and **3b** is dissolved in ± 2840 mL dichloromethane and cooled to O°C under a nitrogen atmosphere. A solution of 1.5 g sodium in 280 dry methanol is added dropwise to this solution. This mixture is stirred for 8 to 10 days at rT. It is recommended to check the pH. If the pH is too low, then fresh sodium in MeOH should be added. The white precipitate is filtered off and is washed with ether and dried to constant weight. Recrystallization from ethanol produces 133.0 g (0.69 mol, 91 %) tetraol **4** as white needles. **IR** (KBr) 3260, 3000, 2960, 2930, 2860, 2780 cm^{-1}; **^{1}H-NMR** (D_6- DMSO, 250 MHz): δ 4.93 (d, J = 6.0 Hz, 1H, OCH_2O), 4.63 (d, J = 6.3 Hz, 1H, OCH_2O), 4.60 (m, 2H, OH), 4.40 (m, 2H, OH), 3.6-3.5 (m, 6H, 1 + 3 + 5 + 6), 3.4-3.3 (m, 2H, 2 + 4). **mp**: 157 - 161° C.

1,3:5,6-Di-*O*-phenylmethylene-2,4-*O*-methylene-D-glucitol 5.

40.04 g (0.21 mol) Of powdered tetraol **4** is suspended in 772 mL cyclohexane. First 52 mL DMF and then 45.71 g (0.43 mol) benzaldehyde and 2 mL H_2SO_4 (98 %) is added to this suspension. The suspension is refluxed using a Dean-Stark apparatus. After a while the suspension will become a transparant solution and then the product will precipitate. After refluxing for ± four hours the suspension is cooled to rT and neutralized with a saturated $NaHCO_3$ solution. Then the precipitate is filtered off and the resulting residue is washed with respectively water and Et_2O. 58.21 g (0.16 mol, 75 %) Of **5** is isolated as white wadding which are an epimeric mixture (in a 9:1 ratio). Recrystallization from EtOH produces **5** as white needles. In seperate batches varying epimeric ratios are observed. **IR** ($CHCl_3$): 3090, 3070, 3030, 3000, 2870, 2770, 1600. Main product: **^{1}H-NMR** ($CDCl_3$, 250 MHz): δ 7.5-7.4 (m, 4H, arom. H), 7.4-7.3 (m, 6H, arom. H), 5.93 (s, 1H, $PhCHO_2$), 5.59 (s, 1H, $PhCHO_2$), 5.27 (d, J = 6.3 Hz, 1H, OCH_2O), 4.85 (d, J = 6.3 Hz, 1H, OCH_2O), 4.5 (m, 1H, 5), 4.34 (dd, J = 12.6 + 1.2 Hz, 1H, 1b), 4.3 - 4.1 (m, 2H, 6), 4.09 (dd, J = 12.7 + 1.8 Hz, 1H, 1a), 4.04 (s, 1H, 3), 3.92 (dd, J = 6.2 + 1.7 Hz, 1H, 4), 3.63 (d, J = 1.3 Hz, 1H, 2). **Microanalysis**: C calcd. 68.11 %, obs. 67.23 %, H calcd. 5.95 %, obs. 6.06 % (1.5 % H_2O). **mp**: 174 - 175° C. Byproduct: **^{1}H-NMR** ($CDCl_3$, 250 MHz): δ 7.5-7.4 (m, 4H, arom. H), 7.4-7.3

(m, 6H, arom. H), 5.78 (s, 1H, PhC<u>H</u>O$_2$), 5.60 (s, 1H, PhC<u>H</u>O$_2$), 5.24 (d, J = 6.3 Hz, 1H, OC$\underline{H}_2$O), 4.83 (d, J = 6.3 Hz, 1H, OC$\underline{H}_2$O), 4.5 (m, 1H, <u>5</u>), 4.4-4.3 (m, 2H, <u>1</u> + <u>6</u>), 4.1-4.0 (m, 2H, <u>1</u> + <u>6</u>), 4.04 (s, 1H, <u>3</u>), 3.70 (dd, J = 7.9 + 1.4 Hz, 1H, <u>4</u>), 3.60 (s, 1H, <u>2</u>). **mp**: 168 - 169° C.

1,3-*O*-Phenylmethylene-2,4-*O*-methylene-D-glucitol <u>6</u>.

A mixture of 60 mL HCO_2H, 360 mL EtOH and 40 mL H_2O is added to a suspension of 5.70 g (15.4 mmol) powdered dibenzylidene derivative **5** in 30 mL EtOH and 90 mL 1,2-dichloroethane. This reaction mixture is refluxed for ± 3.5 hours and the solid dissolves upon heating. (Formation of tetraol **4** is monitored using TLC (eluent: 10 % MeOH in EtOAc).) The reaction mixture is cooled to rT and concentrated under reduced pressure. The residue is three times coëvaporated with toluene. The crude product is recrystallized from EtOH to yield 2.10 g (7.44 mmol, 69 %) of diol **6** as white crystals. **IR** (KBr): 3500, 3480, 3020, 2980, 2940, 2990, 2880, 2790, 1605. **^{1}H-NMR** (D_6-DMSO, 250 MHz): δ 7.5-7.38 (m, 5H, arom. H), 5.64 (s, 1H, PhC<u>H</u>O$_2$), 5.03 (d, J = 6.1 Hz, 1H, OC<u>H</u>$_2$O), 4.80 (d, J = 5.7 Hz, 1H, OH), 4.73 (d, J = 6.2 Hz, 1H, OC$\underline{H}_2$O), 4.38 (t, J = 5.9 Hz, 1H, O<u>H</u>), 4.10 (m, 3H, <u>5</u> + <u>6</u>), 3.69 (m, 2H, <u>1</u> + <u>3</u>), 3.59-3.54 (m, 2H, <u>1</u> + <u>2</u>), 3.44-3.39 (m, 1H, <u>4</u>). **^{13}C-NMR** (D_6-DMSO, 50 MHz; assignment with APT): δ 138.64 (arom. <u>C</u>$_q$), 128.43 + 127.81 + 126.04 (arom. <u>C</u>), 99.22 (Ph<u>C</u>HO$_2$), 91.91 (O<u>C</u>H$_2$O), 69.30 (<u>1</u>), 77.21 + 69.46 + 69.14 + 67.52 (<u>2</u> + <u>3</u> + <u>4</u> + <u>5</u>), 62.52 (<u>6</u>). **Microanalysis**: C calcd. 59.57 %, obs. 59.61 %, H calcd. 6.38 %, obs. 6.53 %. **MS** (EI): accurate mass: obs. 282.1111, calcd. for $C_{14}H_{18}O_6$ 282.1103. **mp**: 188 - 189° C.

***aldehydo*-3,5-*O*-Phenylmethylene-2,4-*O*-methylene-L-xylose <u>7</u>.**

8.283 g (29.27 mmol) Powdered diol **6** is dissolved in 290 mL dioxane. To this solution is added a solution of 7.0405 g (33 mmol) $NaIO_4$ in 290 mL H_2O at rT. After stirring for ± 2 hours at rT (in the mean time the formation of a white precipitate is observed) the reaction mixture is saturated with solid NaCl and filtered off and the residue is washed with dichloromethane. This is extracted with dichloromethane (3x) and the organic layer is washed with a saturated NaCl solution, dried (Na_2SO_4), and concentrated *in vacuo* to yield 6.119 g (24 mmol, 83 %) of the aldehyde **7** as a white solid. **IR** ($CHCl_3$): 3330, 3000, 2850, 2760, 1740. ^{1}H-NMR ($CDCl_3$, 250 MHz): δ 9.67 (s, 1H, <u>1</u>), 7.52-7.42 (m, 2H, arom. H), 5.54 (s, 1H, PhC<u>H</u>O$_2$), 5.34 (d, J = 6.4 Hz, 1H, OC<u>H</u>$_2$O), 4.86 (d, J = 6.4 Hz, 1H, OC$\underline{H}_2$O), 4.34 (dd, J = 12.8 + 1.3 Hz, 1H, <u>5a</u>), 4.30 (s, 1H, <u>2</u>), 4.14-4.06 (d + m, J = 12.8 Hz, 2H, <u>5b</u> + <u>3</u>), 3.62 (d, J = 1.4 Hz, 1H, <u>4</u>). **^{13}C-NMR** ($CDCl_3$, 50 MHz; assignment with APT): δ 199.75 (<u>1</u>), 137.13 (arom. <u>C</u>$_q$), 128.971 + 128.092 + 126.066 (arom. <u>C</u>H), 100.58 (Ph<u>C</u>HO$_2$), 92.44 (O<u>C</u>H$_2$O), 81.514 + 71.38 + 69.25 (<u>2</u> + <u>3</u> + <u>4</u>), 69.79 (<u>5</u>). **Microanalysis**: C calcd. 58.21 %, obs. 58.41 %, H calcd. 6.01 %, obs. 6.22 %. **MS** (EI): accurate mass: obs. 250.0819, calcd. for $C_{13}H_{18}O_5$ 250.0841. **mp**: 165 - 166 ° C.

1,3-Bis((Z)-1,2-dideoxy-4,6-*O*-phenylmethylene-3,5-*O*-methylene-L-*xylo*-hex-1-enitolyl)-benzene <u>8a</u>.

At rT and under a nitrogen atmosphere 16.0 mL (25.6 mmol) of a 1.6 M solution of BuLi in hexane is added slowly to a suspension of 9.183 g (11.7 mmol) of *m*-xylylene-bis(triphenylfosfonium bromide) in 200 mL THF. The resulting red coloured mixture is stirred for one hour at rT. Then a solution of 5.83 g (23.22 mmol) aldehyde **7** in 750 mL THF is added dropwise (within ± three hours) to this mixture. During the addition of the aldehyde solution to the bisylide mixture the red colour changes succesively to an orange, a yellow and finally to white colour. The reaction is quenched with a water/THF mixture. The reaction mixture is partially concentrated *in vacuo* and 200 mL of a saturated NaCl solution is added to the residue. This mixture is extracted with dichloromethane and then dried (Na_2SO_4) and the precipitate filtered off to give the crude product **8** after concentration *in vacuo*. The crude product is stirred with a small amount MeOH to produce after filtration 4.289 g (7.52 mmol, 65 %) of the condensationproduct **8** as a white powder which consists of a mixture of the Z,Z- **8a** and the Z,E-isomer **8b** in 1:3 ratio. Separation of the isomers can be accomplished using flash chromatography (30 % PE 60-80 in EtOAc as eluent). This Wittig reaction is also carried out under other reactionconditions. There have been applied various bases, various solvents and various temperatures to do this condensation reaction. On a big scale the afore mentioned experimental instruction gives the best results. The reactions are all carried out with dried solvents and under a nitrogen atmosphere. The K_2CO_3 used is dried in an oven (300 °C) during 48 hours. Respectively is mentioned: mmol aldehyd **5**; molequivalents base; temperature; yield; solvent ; Z,Z : Z,E. *a)* 1.26 mmol; LDA (2.2); - 20 °C; 48 %; 80 mL THF; 2 : 1. *b)* 1.69 mmol; BuLi (2.2); rT; 72 %; 48 mL THF; 1 : 3. *c)* 3.13 mmol; K_2CO_3 (2.2); rT; 72 %; 42 mL DMF; >10 : 1. *d)* 0.5 mmol; K_2CO_3 (2.2); rT; 46 %; 6 mL CH_3CN; 3 : 1. *e)* 0.5 mmol; KO^{t}Bu (2.2); rT; 10 %; 4 mL DMF; >10 : 1. Z,E -isomer **8b**: **IR**

($CHCl_3$): 3020, 3000, 2940, 2860, 2760. **^{1}H-NMR** ($CDCl_3$, 250 MHz): δ 7.6-7.5 (m, 4H, arom. H), 7.4-7.1 (m, 10H, arom. H), 6.7 (m, 2H, 1(Z) + 1(E)), 6.43 (dd, J = 16.0 + 6.91 Hz, 1H, 2(E)), 6.14 (dd, J = 11.6 + 9.07 Hz, 1H, 2(Z)), 5.56 (s, 1H, $PhCHO_2$), 5.53 (s, 1H, $PhCHO_2$), 5.31 (d, J = 6.35 Hz, 1H, OCH_2O), 5.22 (d, J = 6.32 Hz, 1H, OCH_2O), 4.92 (d, J = 6.39 Hz, 1H, OCH_2O), 4.79 (d, J = 6.33 Hz, 1H, OCH_2O), 4.47 (d, J = 9.70 Hz, 1H, 3(Z)), 4.3-4.2 (m, 3H, 3(E) + 6b(Z) + 6b(E)), 4.09 (dd, J = 12.7 + 1.77 Hz, 1H, 6a(E)), 3.99 (dd, J = 12.6 + 1.80 Hz, 1H, 6a(Z)), 3.90 (bs, 1H, 4(E)), 3.75 (bs, 1H, 4(Z)), 3.67 (bs, 1H, 5(E)), 3.46 (bs, 1H, 5(Z)). **^{13}C-NMR** ($CDCl_3$, 50 MHz; assignment with APT): δ 137.80 + 136.78 + 136.69 (arom. C_q), 133.94 + 133.18 (1(Z) + 1(E)), 128.96 + 128.89 + 128.53 + 128.11 + 127.81 + 126.53 + 126.26 + 126.05 + 125.97 + 125.69 + 125.11 (arom. CH), 100.98 + 100.90 + 100.83 (O_2CHPh), 93.05 + 92.71 (OCH_2O), 79.51 + 74.48 + 73.24 + 72.73 + 69.95 + 69.77 (3(Z) + 4(Z) + 5(Z) + 3(E) + 4(E) + 5 (E)), 70.01 (6). **mp**: 230 - 233 ° C. Z,Z-isomer **8a**: **IR** ($CHCl_3$): 3000, 2860, 2765. **^{1}H-NMR** ($CDCl_3$, 250 MHz): δ 7.6-7.5 (m, 4H, arom. H), 7.4-7.2 (m, 10H, arom. H), 6.76 (d, J = 11.7 Hz, 2H, 1), 6.18 (dd, J = 11.6 + 9.07 Hz, 2H, 2), 5.57 (s, 2H, $PhCHO_2$), 5.26 (d, J = 6.37 Hz, 2H, OCH_2O), 4.86 (d, J = 6.43 Hz, 2H, OCH_2O), 4.51 (d, J = 8.97 Hz, 2H, 3), 4.32 (dd, J = 12.6 + 0.78 Hz, 2H, 6b), 4.04 (dd, J = 12.6 + 1.70 Hz, 2H, 6a), 3.79 (bs, 2H, 4), 3.55 (bs, 2H, 5). **^{13}C-NMR** ($CDCl_3$, 50 MHz; assignment with APT): δ 137.79 + 136.68 (arom. C_q + arom. C_q (Ph)), 133.93 (1), 128.95 + 128.88 + 128.52 + 128.10 + 127.80 + 126.53 + 126.25 (arom. CH + 2), 100.89 ($PhCHO_2$), 92.70 (OCH_2O), 74.48 + 72.72 + 69.76 (3 + 4 + 5), 70.07 (6). **mp**: 235 - 237 ° C.

1,3-Bis(1,2-dideoxy-4,6-*O*-phenylmethylene-3,5-*O*-methylene-L-*xylo*-(hexitolyl)-benzene 9.

394 mg (0.69 mmol) Of the unsaturated compound **8** is dissolved in a suspension of 40 mg of 10 % Pd/C in 35 ml dichloromethane. After hydrogenating for two hours under atmospheric pressure, there is no starting material observable on TLC. The reaction mixture is filtered off using Celite® and the residue is washed with dichloromethane and this produces after concentration *in vacuo* 325 mg (0.56 mmol, 82 %) of the hydrogenated product **9** as a white solid. Pure product can be obtained by recrystallization from EtOAc. **IR** ($CHCl_3$): 3000, 2960, 2860, 2770. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ 7.56-7.51 (m, 4H, arom. H), 7.39-7.19 (m, 7H, arom. H), 7.06-7.04 (m, 3H, arom. H), 5.53 (s, 2H, $PhCHO_2$), 5.25 (d, J = 6.3 Hz, 2H, OCH_2O), 4.78 (d, J = 6.3 Hz, 2H, OCH_2O), 4.34 (dd, J = 12.6 + 1.2 Hz, 2H, 6a), 4.05 (dd, J = 12.6 + 1.9 Hz, 2H, 6b), 3.70 (s, 2H, 4), 3.65-3.60 (m, 2H, 3), 3.53 (d, J = 1.2 Hz, 2H, 5), 2.87-2.73 (m, 2H, 1a), 2.70-2.59 (m, 2H, 1b), 2.33-2.21 (m, 2H, 2a), 2.19-1.84 (m, 2H, 2b). **^{13}C-NMR** ($CDCl_3$, 50 MHz; assignment with APT): δ 141.78 + 137.92 (2x arom. C_q), 128.53 + 128.23 + 127.81 + 125.96 + 125.90 (arom. CH), 100.43 ($PhCHO_2$), 92.91 (OCH_2O), 77.16 + 72.15 + 69.81 (3 + 4 + 5), 69.84 (6), 31.75 (2), 31.72 (1). **mp**: 218 - 220° C. $[\alpha]_D$ - 64.1° (c 1.08, dichloromethane).

1,3-Bis(1,2-dideoxy-4-*O*-phenylmethyl-3,5-*O*-methylene-L-*xylo*-hexitolyl)-benzene 10.

Under a nitrogen atmosphere 132 mg $LiAlH_4$ (3.48 mmol) and 19 mL dry Et_2O is added to a solution of 200 mg (0.25 mmol) of compound **9** in 31 mL dry dichloromethane. Then the reaction mixture is heated to reflux temperature. Then under a nitrogen atmosphere an icecold solution of 495 mg (3.71 mmmol) of $AlCl_3$ in dry Et_2O is added dropwise to the refluxing reaction mixture. The reaction is complete after three hours of refluxing and is quenched carefully with 3 mL MeOH/H_2O (1:1) while cooling with an icebath. Then the reaction suspension is filtered over Celite® and the filtrate is concentrated *in vacuo*. To the residue is added a saturated NaCl solution and this is extracted (3x) with dichloromethane to yield the crude product after drying (Na_2SO_4) and concentration *in vacuo*. Flash chromatography (eluent 10 % PE in EtOAc) yields 134 mg (0.23 mmol, 67 %) diol **10** as a transparant oil which crystallizes on standing. **IR** ($CHCl_3$): 3600, 3500, 3000, 2950, 2850, 2770. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ 7.36-7.20 (m, 11H, arom. H), 7.02-6.97 (m, 3H, arom. H), 5.22 (d, J = 6.1 Hz, 2H, OCH_2O), 4.75 (d, J = 6.1 Hz, 2H, OCH_2O), 4.69 (d, J = 11.5 Hz, 2H, CH_2Ph), 4.56 (d, J = 11.5 Hz, 2H, OCH_2Ph), 3.81 (ddd, J = 10.8 + 7.1 + 3.6 Hz, 2H, 6a), 3.68 (m, 2H, 5), 3.57-3.47 (m, 4H, 3 + 6b), 3.31 (s, 2H, 4), 2.85-2.75 (m, 2H, 1a), 2.67-2.56 (m, 2H, 1b), 2.25-2.16 (m, 2H, 2a), 1.75-1.62 (m, 4H, 2b + OH (2x)). **^{13}C-NMR** ($CDCl_3$, 50 MHz; assignment with APT): δ 141.71 + 137.48 (2x arom. C_q), 128.75 + 128.65 + 128.49 + 128.37 + 128.18 + 126.09 (arom. CH), 93.67 (OCH_2O), 80.07 + 78.92 (3 + 5), 75.04 (OCH_2Ph), 73.44 (4), 62.31 (6), 33.07 (2), 31.25 (1). **Microanalysis**: C calcd. 70.59 %, obs. 69.15 %, H calcd. 7.27 %, obs. 7.32 %, (1.5 % H_2O). **MS** (FAB): accurate mass: obs. 601.2786, calcd. for $C_{34}H_{42}O_8Na$ 601.2777. **mp**: 120-123 °C.

(4R,8S,21S,25R,33S,34S)-33,34-di(phenylmethoxy)-5,7,10,13,16,19,22,24-octaotetracyclo [26.3.1.1^{4,8}.1^{21,25}]tetratriaconta-1(32),28,30-triene 1b.

Under a nitrogen atmosphere 91 mg NaH (55 % dispersion, 2.1 mmol) is washed (3x) with dry pentane and then 10 mL dry THF is added and this suspension is heated to reflux temperature. A solution of 400 mg (0.69 mmol) diol **10** and 316 mg (0.69 mmol) triethyleneglycolditosylate in 25 mL dry THF is added dropwise in three hours to the refluxing solution. After 48 hours the reaction is carefully quenched with a 1:1 H_2O/THF mixture. This mixture is partially concentrated *in vacuo* and a saturated NaCl solution is added to the residue and then this mixture is extracted with EtOAc (2x) and dichloromethane (3x) to give 547 mg crude product. Flash chromatography using 25 % PE in EtOAc as eluent gives 206 mg (0.30 mmol, 43 %) of the macrocyclic product **1b** as a transparant oil. This macrocyclization is also carried out with KH (35 % dispersion) as base with a yield of 39 % of product **1b** with identical spectral data. **IR** ($CHCl_3$): 3040, 3020, 3000, 2950, 2920, 2860, 2770, 1610. **^{1}H-NMR** (C_6D_6, 300 MHz): δ 7.49 (d, J = 7.3 Hz, 4H, arom. H), 7.41-7.00 (m, 7H, arom. H + 30), 6.98 (m, 3H, 29 + 31 + 32), 5.11 (d, J = 5.9 Hz, 2H, 6a + 23a), 4.70 (d, J = 11.8 Hz, 2H, OCH_2Ph), 4.60 (d, J = 11.8 Hz, 2H, OCH_2Ph), 4.45 (d, J = 6.0 Hz, 2H, 6b + 23b), 3.69-3.59 + 3.54-3.43 + 3.40- 3.16 (m (3x), resp. 4H + 4H + 10H, 4 + 8 + 9 + 11 + 12 + 14 + 15 + 17 + 18 + 20 + 21 + 25), 3.11 (s, 2H, 33 + 34), 2.83-2.73 (m, 2H, 2a + 27a), 2.68-2.60 (m, 2H, 2b + 27b), 2.43- 2.31 (m, 2H, 3a + 26a), 1.54-1.43 (m, 2H, 3b + 26b). **^{13}C-NMR** ($CDCl_3$, 50 MHz; assignment with APT): δ 141.37 (1 + 28), 137.94 (arom. C_q Bn), 129.20 + 128.64 + 128.50 + 128.29 + 127.82 + 126.51 (29 + 30 + 31 + 32 + arom. CH Bn), 93.58 (6 + 23), 78.20 + 76.88 (4 + 25 + 8 + 21), 73.24 (OCH_2Ph), 73.24 (33 + 34), 70.92 + 70.78 + 70.34 (11 + 12 + 14 + 15 + 17 + 18), 69.65 (9 + 20), 32.87 (3 + 26) + 30.21 (2 + 27). **MS** (FAB): accurate mass: obs. 715.3449, calcd. for $C_{40}H_{52}O_{10}Na$ 715.3458. $[\alpha]_D$ - 20.0° (c 9.60, dichloromethane).

(4R,8S,24S,28R,36S,37S)-36,37-Di(phenylmethoxy)-5,7,10,13,16,19,22,25,27-nonaoxatetracyclo [29.3.1.1^{4,8}.1^{24,28}]heptatriaconta-1(35),31,33-triene 1c.

Under a nitrogen atmosphere 45 mg NaH (55 % dispersie, 1.0 mmol) is washed (3x) with dry pentane and then 5 mL dry THF is added and this suspension is heated to reflux temperature. A solution of 202 mg (0.35 mmol) of diol **10** and 174 mg (0.35 mmol) tetraethyleneglycolditosylate in 12 mL dry THF is added dropwise in three hours to the refluxing solution. After 48 hours the reaction is carefully quenched with a 1:1 H_2O/THF mixture. The crude product is partially concentrated *in vacuo* and a saturated NaCl solution is added to the residue and that mixture is extracted with EtOAc (2x) and dichloromethane (3x) to give after respectively combination of the organic layers, drying (Na_2SO_4) and concentration *in vacuo* 230 mg of the crude product. Flash chromatography with EtOAc and then with 10 % EtOH in EtOAc yields 53 mg (0.072 mmol, 21 %) of the macrocyclic product **1c** as a transparant oil and also 58 mg (0.039 mmol, 23 %) of product **1g** as a transparant oil that is probably the 2 + 2 macrocyclizationproduct. This macrocyclization is also carried out with KH (35 % dispersion) as base with a yield of 18 % of product **1c** with identical spectral data. Product **1c**: **IR** ($CHCl_3$): 3000, 2940, 2905, 2760, 2770, 1610. **^{1}H-NMR** ($CDCl_3$, 200 MHz): δ 7.18 (m, 1H, arom. H), 6.98 (m, 2H, arom. H), 6.82 (m, 1H, arom. H), 5.17 (d, J = 6.0 Hz, 2H, 6a + 26a), 4.73 (d, J = 11.4 Hz, 2H, OCH_2Ph), 4.69 (d, J = 5.9 Hz, 2H, 6b + 26b), 4.62 (d, J = 11.4 Hz, 2H, OCH_2Ph), 3.83-3.36 (m, 24H, 4 + 8 + 9 + 11 + 12 + 14 + 15 + 17 + 18 + 20 + 21 + 23 + 24 + 28), 3.36 (s, 2H, 36 + 37), 2.69-2.60 (m, 4H, 2 + 30), 2.20-2.04 (m, 2H, 3a + 29a), 1.52-1.45 (m, 2H, 3b + 29b). **^{13}C-NMR** ($CDCl_3$, 50 MHz; assignment with APT): δ 141.57 (1 + 31), 138.08 (C_q Bn), 128.68 + 128.51 + 128.40 + 128.24 + 127.71 + 126.27 (32 + 33 + 34 + 35 + arom. CH Bn), 93.58 (6 + 26), 77.97 + 77.85 (4 + 24 + 8 + 28), 74.81 (OCH_2Ph), 73.24 (36 + 37), 70.75 + 70.57 + 70.47 + 69.19 (11 + 12 + 14 + 15 + 17 + 18 + 20 + 21), 32.85 (3 + 29), 30.67 (2 + 30). **MS** (FAB): accurate mass: obs. 759.3705, calcd. for $C_{42}H_{56}O_{11}Na$ 759.3720. $[\alpha]_D$ - 18.8° (c 2.80, $CHCl_3$). Product **1g**: **IR** ($CHCl_3$): 3000, 2940, 2900, 2860, 2770, 1610. **^{1}H-NMR** ($CDCl_3$, 200 MHz): δ 7.34-7.22 (m, 20H, arom. H (Ph)), 7.17 + 6.95-6.89 (m + m, 2H + 6H, arom. H), 5.17 (d, J = 6.0 Hz, 2H, OCH_2O), 4.73 (d, J = 6.1 Hz, 4H, OCH_2O), 4.63 (s, 8H, OCH_2Ph), 3.85-3.35 (m, 52H, OCH (12x) + OCH_2 (20x)), 3.35 (s, 4H, BnOCH), 2.72-2.51 (m, 8H, CH_2CH_2Ar), 2.17-2.08 (m, 4H, CH_2CH_2Ar), 1.71-1.55 (m, 4H, CH_2CH_2Ar). **^{13}C-NMR** ($CDCl_3$, 75.5 MHz; assignment with APT): δ 141.70 (arom. C_q), 137.96 (arom. C_q Bn), 128.66 + 128.58 + 128.48 + 128.31 + 127.86 + 125.99 (arom. CH+ arom. CH Ph), 93.60 (OCH_2O), 78.77 + 78.23 + 73.26 (CHO), 74.92 (OCH_2Ph), 70.66 + 70.51 + 70.36 + 69.86 (CCH_2O), 32.97 (CH_2CH_2Ar), 31.14 (CH_2CH_2Ar). $[\alpha]_D$ -11.0° (c 1.53, $CHCl_3$).

(4R,8S,21S,25R,33S,34S)-33,34-Dihydroxy-5,7,10,13,16,19,22,24-octaoxatetracyclo [26.3.1.1^{4,8}.1^{21,25}]tetratriaconta-1(32),28,30-triene 1a.

To a solution of 178 mg (0.26 mmol) of the macrocyclic product **1b** in 20 mL EtOH is added 35 mg 10 % Pd/C. During 4 hours this suspension is hydrogenated under a 55 psi pressure. The reaction mixture is filtered off using Celite® and the residue is washed with EtOH and dichloromethane to yield after concentration *in vacuo* 130 mg (0.25 mmol, 99 %) of diol **1a** as a transparant oil. **IR** ($CHCl_3$): 3560, 3000, 2940, 2860. **^{1}H-NMR** (C_6D_6, 300 MHz; assignment with COSY): δ 7.15 (30 under C_6D_6), 7.09 (s, 1H, 34), 6.97 (m, 2H, 29 + 31), 5.05 (d, J = 6.1 Hz, 2H, 6a + 23a), 4.55 (d, J = 6.1 Hz, 2H, 6b + 23b), 3.73-3.65 (m, 2H, 9a + 20a), 3.60-3.52 (m, 4H, 9b + 20b + 8 + 21), 3.40- 3.10 (m, 18H, 4 + 11 + 21 + 14 + 15 + 17 + 18 + 20 + 25 + 33 + 34 + OH (2x)), 2.83-2.74 (m, 2H, 2a + 27a), 2.70-2.60 (m, 2H, 2b + 27b), 2.40-2.28 + 1.70-1.59 (m (2x), 2H (2x), 3 + 26). **^{13}C-NMR** (C_6D_6, 50 MHz; assignment with APT, COSY, ^{13}C-^{1}H corr.): δ 142.95 (1 + 28), 130.51 (30) + 129.65 (32)+ 127.23 (29 + 31), 94.58 (6 + 23), 79.80 (8 + 21), 79.25 + 67.14 (4 + 25 + 33 + 34), 71.93 + 71.67 + 71.50 (11 + 12 + 14 + 15 + 17 + 18), 71.33 (9 + 20), 34.18 (3 + 26), 31.88 (2 + 27). **MS** (FAB): accurate mass: obs. 535.2530, calcd. for $C_{26}H_{40}O_{10}Na$ 535.2519. $[\alpha]_D$ + 22.5° (c 1.55, $CHCl_3$).

(4R,8S,21S,25R,33S,34S)-33,34-Dimethoxy-5,7,10,13,16,19,22,24-octaoxatetracyclo [26.3.1.1^{4,8}.1^{21,25}]tetratriaconta-1(32),28,30-triene 1d.

Under a nitrogen atmosphere a solution of 125 mg (0.15 mmol) of diol **1a** in 0.7 mL dry DMF is added dropwise to a suspension of 16 mg NaH (60 % dispersion, 0.4 mmol) in 0.2 mL DMF. The NaH-dispersion is washed before use with dry pentane. This suspension is stirred at rT for 30 minutes and then 21 µL (48 mg, 0.34 mmol) of MeI is added slowly. This reaction mixture is stirred for 4 hours. When on TLC no starting material is observable, the reaction is quenched with a saturated NH_4Cl solution. This mixture is extracted with Et_2O and then with dichloromethane to give after drying (Na_2SO_4), filtering off the precipitate and concentration *in vacuo* of the combined organic layers 75 mg (0.135 mmol, 90 %) of the macrocyclic compound **1d** as a white solid. **IR** ($CHCl_3$): 3060, 3040, 3000, 2930, 2900, 2860, 2760. **^{1}H-NMR** ($CDCl_3$, 200 MHz): δ 7.19 (m, 1H, 30), 7.01 (m, 1H, 32), 6.96 (m, 2H, 29 + 31), 5.15 (d, J = 6.03 Hz, 2H, 6a + 23a), 4.65 (d, J = 6.1 Hz, 2H, 6b + 23b), 3.74-3.33 (m, 26H, 4 + 8 + 9 + 11 + 12 + 14 + 15 + 17 + 18 + 20 + 21 + 25 + MeO (2x)), 3.49 (s, 6H, MeO (2x)), 2.96 (s, 2H, 33 + 34), 2.86-2.62 (m, 4H, 2 + 27), 2.34- 2.16 (m, 2H, 3a + 26a), 1.69-1.53 (m, 2H, 3b + 26b). **^{13}C-NMR** ($CDCl_3$, 50 MHz; assignment with APT): δ 141.53 (1 + 28), 128.95 + 128.64 + 126.43 (29 + 30 + 31 + 32), 93.51 (6 + 23), 78.15 + 77.49 (4 + 25 + 8 + 21), 75.76 (33 + 34), 70.89 + 70.71 + 70.31 (11 + 12 + 14 + 15 + 17 + 18), 69.51 (9 + 20), 61.35 (CH_3O), 32.89 (3 + 26) + 30.21 (2 + 27). **MS** (FAB): accurate mass: obs. 541.3003, calcd. for $C_{28}H_{45}O_{10}$ 541.3013. **mp**: 148-149 °C. $[\alpha]_D$ + 24.7° (c 2.07, dichloromethane).

(4R,8S,24S,28R,36S,37S)-36,37-Dimethoxy-5,7,10,13,16,19,22,25,27-nonaoxatetracyclo [29.3.1.1^{4,8}.1^{24,28}]heptatriaconta-1(35),31,33-triene 1e.

To a solution of 47 mg (0.095 mmol) of the macrocyclic product **1c** in 10 mL EtOH is added 10 mg 10 % Pd/C. During 24 hours this suspension is hydrogenated under a 55 psi pressure. The suspension is filtered off using Celite® and the resulting residue is washed with EtOH and dichloromethane to give after concentration *in vacuo* 39 mg of diol **1f** (0.07 mmol, 74 %). Then under N_2 at rT a solution of 18 mg (0.032 mmol) diol **1f** in 0.4 mL dry DMF is added to a suspension of 4 mg NaH (60 % dispersion, 0.1 mmol) in 0.1 mL DMF. The NaH-dispersion is washed with dry pentane before use. This suspension is stirred at rT for 30 minutes and then 5 µL (11.5 mg, 0.081 mmol) of MeI is added dropwise. This is stirred for 4 hours and if on TLC no starting material is observable the reaction is quenched with a saturated NH_4Cl solution. This mixture is extracted with Et_2O and dichloromethane to yield, after drying (Na_2SO_4), filtering off the precipitate and concentration *in vacuo* of the combined organic layers, 18.4 mg (0.032 mmol, 100 %) of the macrocyclic compound **1e** as a transparant oil. **IR** ($CHCl_3$): 2990, 2880, 2840, 2740. **^{1}H-NMR** ($CDCl_3$, 200 MHz): δ 7.24 (m, 1H, 33), 7.05 (m, 1H, 35), 7.02 (m, 2H, 32 + 34), 5.13 (d, J = 6.0 Hz, 2H, 6a + 26a), 4.69 (d, J = 6.1 Hz, 2H, 6b + 26b), 3.87-3.20 (m, 30H, 4 + 8 + 9 + 11 + 12 + 14 + 15 + 17 + 18 + 20 + 21 + 23 + 24 + 28 + MeO (2x)), 3.52 (s, 6H, MeO (2x)), 3.07 (s, 2H, 36 + 37), 2.85-2.61 (m, 4H, 2 + 30), 2.33- 2.15 (m, 2H, 3a + 29a), 1.80-1.63 (m, 2H, 3b + 30b). **^{13}C-NMR** ($CDCl_3$, 62.9 MHz; assignment with APT, DEPT): δ 141.73 (1 + 31), 128.79 + 128.64 + 126.39 (32 + 33 + 34 + 35), 93.62 (6 + 26), 78.10 + 78.01 (4 + 28 + 8 + 24), 75.55 (36 + 37), 70.88 + 70.70 + 70.63 + 70.56 (11 + 12 + 14 + 15 + 17 + 18 + 20 + 21), 69.30 (9 + 23), 61.41 (CH_3O), 32.97 (3 + 29) + 31.04 (2 + 30). **MS** (FAB): 607 ($[M + Na]^+$). $[\alpha]_D$ + 23.6° (c 1.05, dichloromethane).

5-*O*-Trityl-D-xylose diethylthioacetal 12.

To a solution of 15 g (58.6 mmol) of the D-xylose thioacetal[10] **11** in 225 mL dichloromethane is added 30 mL Et_3N, 100 mg DMAP and 18 g (64.5 mmol) tritylchloride. After stirring this mixture for 48 hours at rT this is poured into icecold water and this is stirred for another 30 minutes. The organic layer is washed with a saturated NH_4Cl solution, a saturated NaCl solution and is finally concentrated *in vacuo*. Purification using flash chromatography (PE:EtOAc = 1:1) yields 24.4 g (49 mmol, 84 %) of the thioacetal **12** as a dark oil. **IR** ($CHCl_3$): 3560-3460, 3040, 3000, 2975, 2930, 2875, 1590. **^{1}H-NMR** ($CDCl_3$, 250 MHz): δ 7.50-7.43 (m, 6H, arom. H), 7.33-7.19 (m, 9H, arom. H), 4.19 (s, 1H), 4.05 (m, 1H), 3.90 (m, 1H), 3.54 (d, J = 8.8 Hz, 1H), 3.37-3.21 (d (AB), J = 9.6 Hz, 2H, CH_2OTr), 2.70 (m, 4H, SCH_2CH_3), 1.27 + 1.26 (t (2x), 3H (2x), SCH_2CH_3). $[\alpha]_D$ + 27.4° (c 1.17, $CHCl_3$).

2,3,4-Tri-*O*-methyl-5-*O*-trityl-D-xylose diethylthioacetal 13.

Under a nitrogen atmosphere 2.6 g NaH (55 % dispersion, 59.6 mmol) is washed with dry pentane. To this is added 20 mL dry DMF and then the suspension is cooled with an icebath. A solution of 9.2 g (18.4 mmol) of acetal **12** in 90 mL dry DMF is added dropwise and the temperature is brought to rT. After 30 minutes the reaction mixture is cooled again with an icebath and then 3.8 mL (61 mmol) of MeI is added dropwise. This mixture is stirred for two hours at 0 °C and for one hour at rT. The reaction is quenched with a MeOH/H_2O mixture. This is extracted together with Et_2O and H_2O, dried ($MgSO_4$) and concentrated *in vacuo* to give 9.9 g (18 mmol, 99 %) of **13** as a yellow oil which crystallizes on standing. **IR** ($CHCl_3$): 3050, 3000-2960, 2920, 2820, 1490. **^{1}H-NMR** ($CDCl_3$, 250 MHz): δ 7.52-7.45 (m, 6H, arom. H), 7.32-7.18 (m, 9H, arom. H), 3.92-3.88 (m, 2H, 5), 3.6-3.3 (m, 12H, 2 + 3 + 4 + CH_3O (3x)), 3.22-3.15 (m, 1H, 1), 2.76-2.56 (m, 4H, SCH_2CH_3), 1.29-1.20 (m, 6H, SCH_2CH_3). **Microanalysis**: C calcd. 68.85 %, obs. 68.77 %, H calcd. 7.46 %, obs. 7.57 %, S calcd. 11.85 %, obs. 11.44 %. **mp**: 88-89 °C. $[\alpha]_D$ -7.2° (c 1.98, $CHCl_3$).

***aldehydo*-2,3,4-Tri-*O*-methyl-5-trityl-D-xylose 14.**

To a stirring solution of 7.15 g (26.3 mmol) $HgCl_2$[11] in 360 mL MeCN:H_2O (4:1) is added 2.85 g (13.2 mmol) HgO and a solution of 6.6 g (12.2 mmol) of thioacetal **13** in 180 mL MeCN:H_2O (4:1). This mixture is stirred for 15 minutes at rT and then refluxed for 5 hours. Then the solution is cooled, filtered off using Celite®, and the residue is washed with a $CHCl_3$/hexane mixture (1:1). The filtrates are washed with a 5M NH_4OAc solution, water, and a saturated NaCl solution and then dried (Na_2SO_4). The precipitate is filtered off and concentrated *in vacuo* to give 6.0 g (14.2 mmol, 85 %) of aldehyde **14** as an oil. **IR** ($CHCl_3$): 3660, 3500, 3020, 3000, 2930, 2860, 2820, 1720. **^{1}H-NMR** ($CDCl_3$, 200 MHz): δ 9.69 (s, 1H, CHO), 7.50-7.46 (m, 6H, arom. H), 7.36-7.21 (m, 9H, arom. H), 3.86-3.70 (m, 2H, 2 + 3), 3.53-3.48 (m, 1H, 4), 3.43-3.21 (m, 11H, 5 + CH_3O (3x)).

1,3-Bis(1,2-dideoxy-3,4,5-tri-*O*-methyl-D-*xylo*-hexitolyl)benzene 16.

Under a nitrogen atmosphere at rT 1.5 mL (2.4 mmol) of a 1.6 M solution of BuLi in hexane is added slowly to a suspension of 846 mg (0.93 mmol) of *m*-xylylene-bis(triphenylfosfonium bromide) in 20 mL THF. The resulting red coloured mixture is stirred for one hour at rT. A solution of 929 mg (2.2 mmol) of aldehyde **14** in 71 mL THF is added dropwise. The colour changes from red to orange to yellow and finally to white. If the reaction is complete, it is quenched with a H_2O/THF mixture. The reaction mixture is partially concentrated *in vacuo* and to the residue is added 200 mL of a saturated NaCl solution. This is extracted (3x) with dichloromethane. The organic layers are dried (Na_2SO_4), filtered off and concentrated *in vacuo*. Flash chromatography with a PE/EtOAc mixture (v/v, 2:1) gives 665 mg crude product. Then the crude mixture is dissolved in 100 mL of a 9:1 (v/v) mixture of EtOH and a 1M HCl solution. To this mixture is added 52 mg 10 % Pd/C. This suspension is hydrogenated under a 55 psi pressure. Then this is neutralized with solid $NaHCO_3$ and partially concentrated *in vacuo* and gives after adding NaCl, extraction with dichloromethane (3x), and drying (Na_2SO_4), the crude diol **16**. Purification with flash chromatography with eluent 10 % EtOH in dichloromethane yields 202 mg (0.44 mmol, 40 % from the aldehyde) of the diol **16** as an oil. **IR** ($CHCl_3$): 3450, 3020, 2995, 2880, 2820. **^{1}H-NMR** (C_6D_6, 250 MHz, 70 °C): δ 7.02-6.99 (m, 3H, arom. H), 3.76 (dd, J = 11.6 + 4.4 Hz, 2H, 6a), 3.63 (dd, J = 11.6 + 4.5 Hz, 2H, 6b), 3.41-3.16 (m, 24H, 3 + 4 + 5 + CH_3O (6x)), 3.34 + 3.27 + 3.23 (s (3x), 18H, CH_3O (6x)), 2.85-2.59 (m, 4H, 1), 2.31 (bs, 2H, OH (2x)), 2.10-1.96 (m, 2H, 2a), 1.94-1.82 (m, 2H, 2b). **^{13}C-NMR** ($CDCl_3$, 50 MHz; assignment with APT): δ 141.99 (arom. C_q), 128.46 + 128.38 + 126.86 (arom. CH), 82.60 + 81.44 + 79.99 (3 + 4 + 5), 61.30 (6), 60.27 + 58.42 + 57.91 (CH_3O), 31.98 (2), 31.59 (1).

MS (FAB): accurate mass: obs. 459.2965, calcd. for $C_{24}H_{43}O_8$ 459.2958. $[\alpha]_D$ + 4.6° (c 3.80, dichloromethane).

(4S,5R,6R,19R,20R,21S)-4,5,6,19,20,21-Hexamethoxy-8,11,14,17-tetraoxabicyclo[22.3.1]octacosa-1(28),24,26-triene 2.

Under a nitrogen atmosphere 85 mg (55 % dispersion, 1.9 mmol) NaH is washed (3x) with dry pentane and 12 mL dry THF is added and this suspension is heated to reflux temperature. A solution of 300 mg (0.65 mmol) of diol **16** and 300 mg (0.65 mmol) triethyleneglycolditosylate in 23 mL dry THF is added dropwise in three hours to the refluxing solution. After 20 hours of refluxing the reaction is carefully quenched with a 1:1 H_2O/THF mixture. The crude product is partially concentrated *in vacuo* and a saturated NaCl solution is added. Then this mixture is extracted with EtOAc (3x) and gives after drying (Na_2SO_4) and concentration *in vacuo* 547 mg of the crude product. Flash chromatography with 10 % EtOH in dichloromethane gives 171 mg (0.30 mmol, 46 %) of the macrocyclic product **2** as an oil. **IR** ($CHCl_3$): 3000, 2925, 2900, 2820, 1600. **^{1}H-NMR** ($CDCl_3$, 300 MHz): δ 7.25-7.2 (m, 1H, 26), 7.04-7.02 (m, 3H, 25 + 27 + 28), 3.60-3.29 (m, 40H, 4 + 5 + 6 + 7 + 9 + 10 + 12 + 13 + 15 + 16 + 18 + 19 + 20 + 21 + CH_3O (6x)), 3.52 + 3.41 + 3.40 (s (3x), 18H, MeO (6x)), 2.73-2.66 (m, 4H, 2 + 23), 1.90-1.76 (m, 2H, 3 + 22). **^{13}C-NMR** ($CDCl_3$, 50 MHz; assignment with APT, ^{13}C-^{1}H corr.): δ 141.02 (1 + 24), 128.24 + 128.06 + 125.82 (25 + 26 + 27 + 28), 82.63 + 80.47 + 80.24 (4 + 5 + 6 + 19 + 20 + 21), 70.74 + 70.52 + 70.30 + 69.92 (7 + 9 + 10 + 12 + 13 + 15 + 16 + 18), 60.83 + 58.43 + 58.16 (CH_3O), 3187 (3 + 22), 31.29 (2 + 23). **MS** (FAB): accurate mass: obs. 595.3449, calcd. for $C_{30}H_{52}O_{10}Na$ 595.3458. $[\alpha]_D$ - 3.02° (c 12.9, dichloromethane).

Typical **Michael Addition reaction.**

Under a nitrogen atmosphere 2 mL of dry toluene is added to a macrocyclic compound (0.127 mmol) (dried thoroughly by 3x coëvaporation with toluene). This solution is stirred at rT for 30 minutes and then methyl phenylacetaat (**17**) (5.1 mmol) is added dropwise. After stirring for 20 minutes the solution is cooled to -78° C. After stirring for 10 minutes at -78° C a solution of methyl acrylate (**18**) (2.5 mmol) in 1 mL dry toluene is added. The reaction is monitored using TLC (eluent PE:EtOAc=9:1) and the spots are detected with UV (methyl phenylacetate) and anisaldehyde/H_2SO_4 reagent (the product ester (**19**)). The product spot is coloured orange. After 1-2 hours the reaction is quenched with a saturated $NaNH_4$ solution. This mixture is extracted with toluene (3x) and dichloromethane (3x). Then the organic layers are combined and dried (Na_2SO_4), and the precipitate is filtered off to give a solution which contains the crude product. This solution is concentrated *in vacuo* and chromatographed with PE:EtOAc=5:1, 3:1, 1:1 to yield the product and methyl phenylacetate. The column is rinsed thoroughly with 20 % EtOH in dichloromethane to give the macrocyclic catalyst. The ee is monitored by measuring the optical rotation of the product ester (**19**) and comparing that to the literature value[3a].

ACKNOWLEDGEMENT

This work was carried out under auspices of the *Stichting Scheikundig Onderzoek Nederland (S.O.N.)* with financial support of the *Nederlandse Organisatie voor Wetenschappelijk Onderzoek (N.W.O.)*.

REFERENCES

1. (a) Bosnich, B. Ed, *Asymmetric Catalysis*, (Procedings of the NATO Advanced Research Workshops on Asymmetric Catalysis, Sanibel Island, Floride, USA, January 2 - 6, 1984), Martinus Nijhoff Publishers, P.O.Box 322, 3300 AH Dordrecht, 1986.
(b) Morrison, J.D. Ed, *Asymmetric Synthesis*, *5*, Academic Press Inc. Ltd., 24 - 28 Oval Road, London NW1 7DX, 1985.
2. (a) Jolley, S.T.; Bradshaw, J.S.; Izatt, R.M. *J. Heterocyclic. Chem.* **1982**, *19*, 3 - 19.
(b) Stoddart, J.F. Chiral Crown Ethers. In *Top. in Stereochem.* **1987**, *17*, 207 - 288, Eliel, E.L.; Wilen, S.H. Eds, John Wiley & Sons, New York.
3. (a) Cram, D.J.; Sogah, G.D.Y. *J. Chem. Soc. Chem. Comm.* **1981**, 625 - 628.

(b) Cram, D.J.; Sogah, G.D.Y. *J. Am. Chem. Soc.* **1985**, *107*, 8301 - 8302.
(c) Alonso-Lopéz, M.; Martin-Lomas, M.; Penadés, S. *Tetrahedron Lett.* **1986**, *27*, 3551 - 3554.
(d) Alonso-Lopéz, M.; Jimenez-Barbera, J.; Martin-Lopez, M.; Penadés, S. *Tetrahedron* **1988**, *44*, 1535 - 1543.
(e) Aoki, S., Sasaki, S., Koga, K. *Tetrahedron Lett.* **1989**, *30*, 7229 - 7230.
(f) Van Maarschalkerwaart, D.A.H.; Willard, N.P.; Pandit, U.K. *Models in Chem.* **1992**, accepted for publication.

4. (a) Pandit, U.K. *Rec. Trav. Chim. Pays-Bas* **1988**, *107*, 111 - 120.
(b) Pandit, U.K. *Bull. Soc. Chim. Belg.* **1986**, *95*, 987 - 993.

5. (a) Vögtle, F.; Hochberg, R.; Kochendörfer, F.; Windscheif, P.-M.; Volkemann, M.; Jansen, M. *Chem. Ber.* **1990**, *123*, 2181 - 2185.
(b) Nakaya, T.; Imito, M. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1547 - 1551.
(c) Yamamoto, K.; Ikeda, T.; Kitsuki, T.; Okamoto, Y.; Chikamatsu, H.; Nakazaki, M. *J. Chem. Soc. Perk. Trans. I* **1990**, 271 - 276.
(d) Thulin, B.; Wennerstrom, O. *Acta Chem. Scand. Sect. B* **1976**, *30*, 369 - 371.

6. (a) Wanner, M; Willard, N.P.; Koomen, G.-J.; Pandit, U.K. *Tetrahedron* **1987**, *43*, 2549 - 2556.
(b) Van den Bos, J.; Vloon, W.J.; Koomen, G.-J.; Pandit, U.K. *Tedrahedron* **1991**, *47*, 6787 - 6794.

7. Ness, A.T.; Hahn, R.M.; Hudson, C.S. *J. Am. Chem. Soc.* **1944**, *66*, 665 - 670.

8. (a) Clode, D.-M. *Chem. Rev.* **1979**, *79*, 491 - 511.
(b) Angyal, J.; Lawler, J.V. *J. Am. Chem. Soc.* **1944**, *66*, 837 - 838.

9. (a) Liptak, A.; Imre, J.; Harangi, J.; Nanasi, P.; Neszmelyi, A. *Tetrahedron*, **1982**, *38*, 3721 - 3727.
(b) Garegg, P.J. *Pure Appl. Chem.* **1984**, *56*, 845 - 858.

10. Rollin, P.; Pougny, J.-R. *Tetrahedron* **1986**, *42*, 3479 - 3490.

11. Corey, E.J.; Erickson, B.W. *J. Org. Chem.* **1971**, *36*, 3553 - 3560.