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# A Carbohydrate Approach to Polyol Fragments of Amphotericin and the Trienomycin- and Mycotrienin Antibiotics[1]

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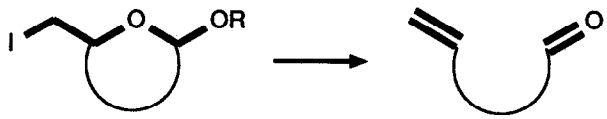
***Abstract:*** Hydrolytically labile ω-chloro-ω-phenylthioglycosides, obtained from the corresponding ω-phenylthioglycosides on treatment with NCS in $CCl_4$, are readily dealkoxyhalogenated with Zn/Ag-graphite in anhydrous solvents affording enantiomerically pure synthons bearing an aldehyde function at the one end and a vinylthioether group at the other end of the ring-opened product. This fragmentation technique turned out to be general and was used for the synthesis of a building block exhibiting the substitution pattern of the C9-C14 segment common to all trienomycin-, mycotrienin- and ansatrienin macrolide antibiotics. Zn/Ag-graphite was also used to reductively ring-open the 6-deoxy-6-iodopyranoside **37**, easily accessible from D-glucose, to enal **38**, which served as central precursor for the synthesis of both the C1-C6 as well as C7-C13 unit of the polyhydroxylated chain of amphoteronolide B. Combining these two segments **45** and **51** by ketophosphonate/aldehyde coupling afforded enone **54** which is synthetically equivalent to an intermediate of a former total synthesis of this macrolide. Thus, a convergent synthesis of the C1-C13 fragment of amphotericin B based upon the hidden $C_2$-symmetry of this target molecule was achieved using metal-graphite promoted ring-opening of carbohydrates in the key step in combination with formal inversion of the configuration of the resulting hex-5-enals.

## INTRODUCTION

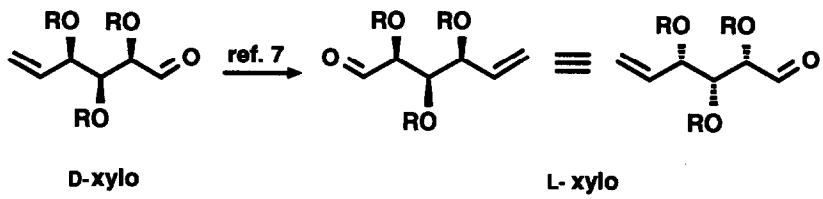
A well established approach to enantiomerically pure compounds is based upon the systematic use of nature's chiral pool comprising *i.a.* carbohydrates, amino- and hydroxy acids and terpenes.[3] This retrosynthetic concept invariably necessitates two consecutive steps: first, disclosing and ascertaining the nearest possible stereochemical relationship between the target molecule and one of the starting materials at hand, and secondly furnishing the substrate chosen with suitable anchor groups for further preparative manipulation. As far as carbohydrates are concerned, this latter duty can be particularly well achieved by reductive ring-opening of deoxyhalo sugars (Scheme 1).[4] This transformation (Vasella reaction) affords building blocks that combine a chiral core region with appropriate functionalities at both ends. In the overall process the monosaccharide's ring-oxygen atom plays a dual role as an internal protecting group

fixing a rigid cyclic structure and as a leaving group in the reductive cleavage process. This allows a flexible interplay of conformationally biased regio- and stereoselective introduction of functional groups in the cyclic precursors followed by a ready switch to an open-chain synthon.




**Scheme 1.** Reductive cleavage of deoxyhalo sugars.

Zinc dust in aqueous alcohol (EtOH, i-PrOH) was initially proposed[4] and widely used[5] for such ring-opening reactions. Only recently, these reactions have been achieved in aprotic solvents (THF, DME) with highly reactive and readily prepared zinc/silver-graphite as the reagent of choice.[6-7] Because of the strictly anhydrous conditions this protocol applies nicely to hydrolytically labile substrates and/or products, which would decompose under the conventional conditions. Moreover, the particularly mild reaction conditions, high yields, simple work-up by filtration,[8] and the improved functional group compatibility are further advantages of this procedure. Its reliability was confirmed in the non-carbohydrate series by Ireland's total synthesis of 9-dihydro FK-506 acetonide.[9]

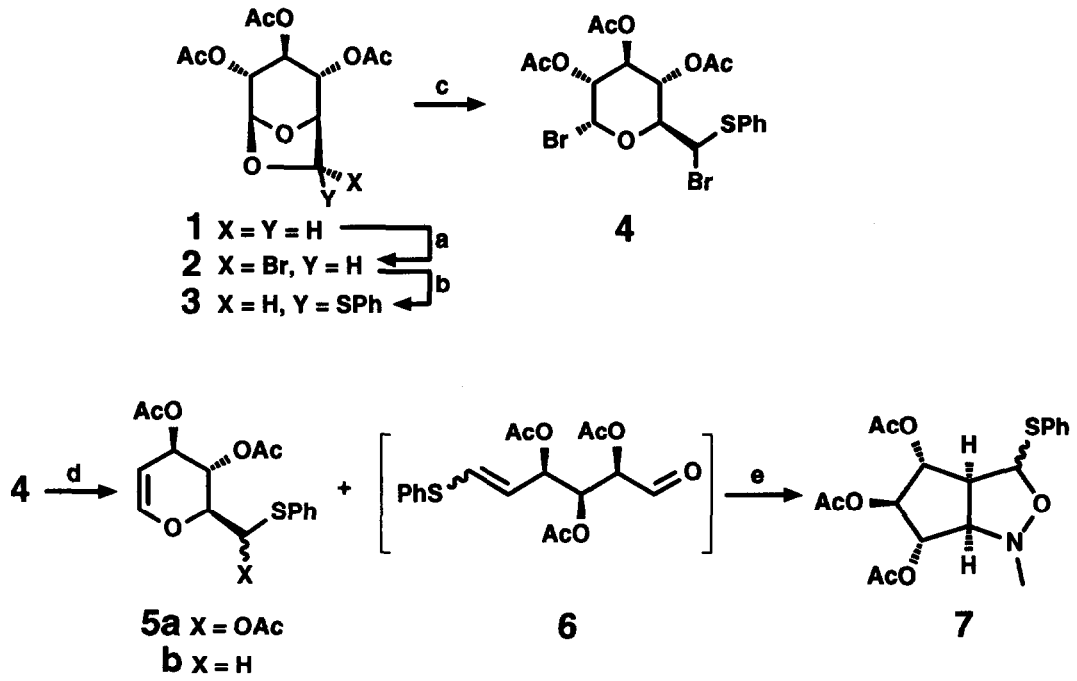



**Scheme 2.** Transposition of enals.[7]

Unfortunately only a rather small number of monosaccarides is available in bulk quantity with particularly few sugars of the L-series among them. This fact severely restricts the use of carbohydrates as enantiomerically pure starting materials in general,[10] and limits the number of sugar-derived hex-5-enals accessible. However, we recently outlined a reaction sequence allowing the ready transposition of the aldehyde and the alkene group in such compounds without passing through any *meso*-intermediate, thereby giving rise to synthons with rare or "unnatural" configurations (Scheme 2).[7] We now report on the application of the zinc/silver-graphite based fragmentation process to the synthesis of macrolide polyol segments in order to further demonstrate what we consider as its main advantages, i.e. the ready transformation of labile compounds and the substantially widened scope by use of enals of otherwise inaccessible configurations.

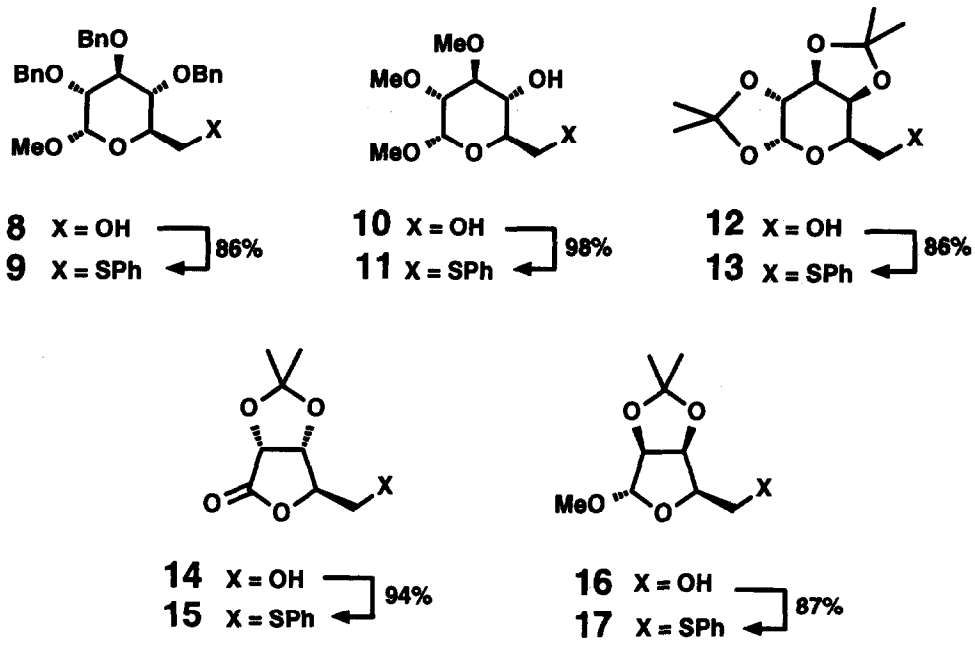
## RESULTS AND DISCUSSION

***α-Chlorothioethers Fragmentation Reactions.*** 6-Bromo-6-phenylthioglucopyranosyl bromide **4** on treatment with zinc dust in acetic acid is known to afford vinyl sulfide **6** as an "indiscrete" intermediate on the pathway to isoxazolidine **7**, together with substantial amounts of the unsaturated by-products **5a** and **5b** (Scheme 3).[5a] Taking into account the well-known propensity of glycosyl bromides to form glycals on reduction with zinc,[11] we assumed that simply switching over to ω-halo-ω-phenylthioglycosides and using aprotic conditions during the dealkoxyhalogenation reaction might suppress these side-reactions and hence render this type of transformation more general. Vinyl sulfides such as **6**, however, as masked dicarbonyl compounds with a substitution pattern unequivocally defined by the configuration of the monosaccharide employed, should be attractive intermediates in natural product synthesis (vide infra).




**Scheme 3.** Literature precedence for vinyl sulfide formation by reductive ring opening of carbohydrates:[5a] (a) NBS; (b) $PhS^-$; (c) HBr, HOAc; (d) Zn dust, HOAc; (e) MeNHOH.

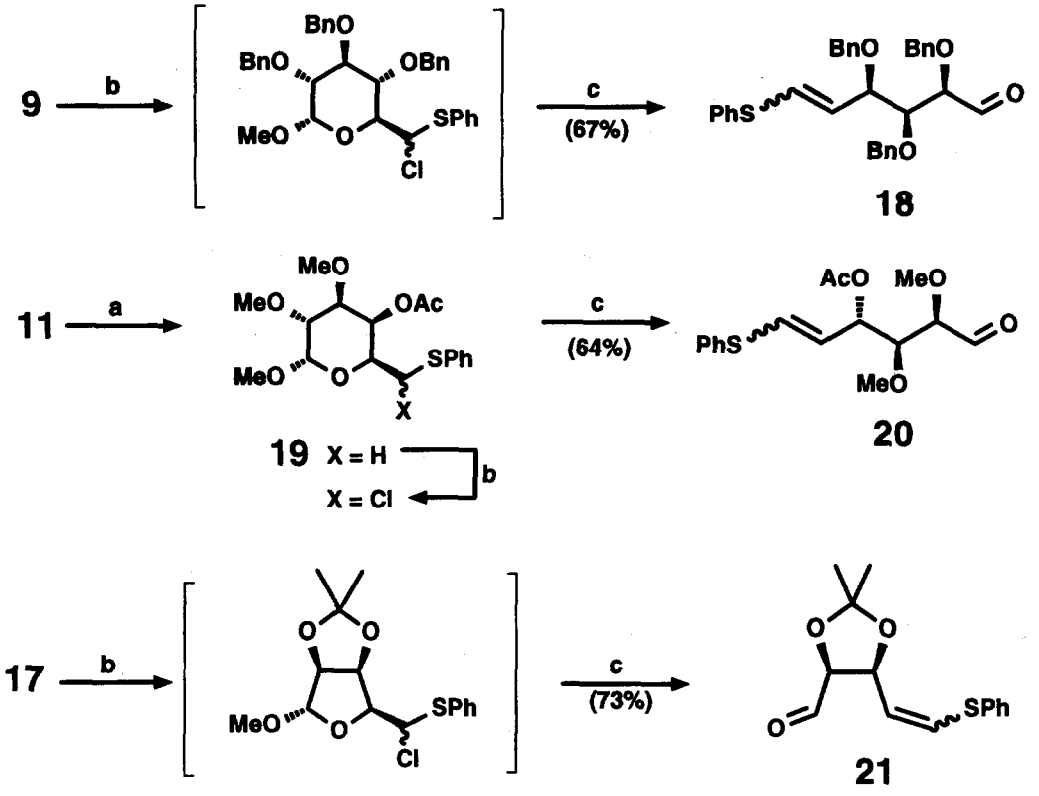
First of all, good access to the ω-halo-ω-phenylthioglycosides as the substrates for the envisaged ring-opening reactions was called for. Whereas dibromide **4** had been obtained from 1,6-anhydroglucopyranose **1** by a sequence of radical bromination (**1**→**2**), -SPh for -Br exchange (**2**→**3**) and opening of the 1,6-anhydro ring with HBr/HOAc (**3**→**4**),[5a] we considered the halogenation of phenylthioethers with N-chlorosuccinimide (NCS)[12] to be a more appropriate approach.




**Scheme 4.** Preparation of carbohydrate derived phenylthioethers using PhSSPh/$Bu_3P$ in pyridine as reagent combination.

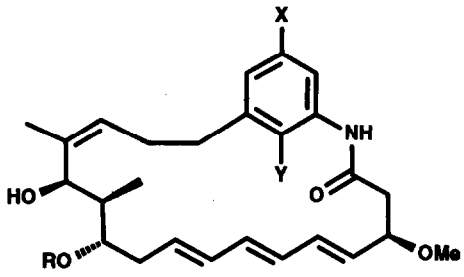
Differently protected phenylthioglycosides **9**, **11**, **13**, **15** and **17** were prepared from the parent sugars using diphenyl disulfide (1.2 equiv.)/$Bu_3P$ (2 equiv.) in pyridine as reagents in good yields at room temperature. In contrast to the previous reports,[13] both the use of a larger molar excess of this noxious mixture as well as the application of high pressure (10 kbar) previously emphasized to promote such thioether formations[13b] turned out to be absolutely unnecessary. Under our conditions only the primary -OH group of diol **10** was substituted by -SPh.

Phenylthioethers **9** and **19** as model compounds for the trienomycin study (vide infra) were smoothly halogenated with NCS in anhydrous $CCl_4$ at or sightly above room temperature. Since the resulting α-chlorothioethers turned out to be prone to hydrolysis, attempted isolation resulted in disappointingly low yields. However, evaporation of the $CCl_4$ and treatment of the crude α-chlorothioether with freshly prepared zinc/silver-graphite[6] in anhydrous THF or DME gave clean conversions to the expected open-chain derivatives **18** and **20**, respectively (Scheme 5). These compounds were obtained as mixtures of the (Z)- and (E)-isomers (for the ratios *c.f.* experimental), which slowly decomposed upon storage in a refrigerator. Although 5-deoxy-5-halofuranose derivatives generally undergo reductive ring-opening more reluctantly,[6] it is worth mentioning that compound **17** was also cleaved without difficulty.



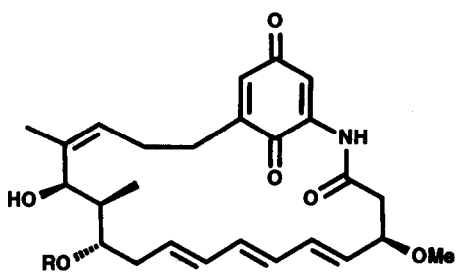

**Scheme 5.** Preparation and reductive cleavage of α-chlorothioethers with Zn/Ag-graphite: (a) (i) triflic anhydride, pyridine; (ii) $Bu_4N^+$ $AcO^-$; MeCN, 80% (both steps); (b) NCS, $CCl_4$; (c) Zn/Ag-graphite, THF or DME.

***The C9-C14 Fragment of the Trienomycin- and Mycotrienin Antibiotics.*** The trienomycin-, mycotrienin- and ansatrienin antibiotics, which are produced by *Streptomyces rishiriensis* and *Streptomyces collinus*, exhibit strong cytotoxicity in vitro against $HeLaS_3$ cells as well as antifungal activity.[14] All members of this group of macrolides share common structural features. One is the homochiral C9-C14 fragment of the *ansa*-chain, the stereochemistry of which has recently been established by the synthesis of both possible enantiomers and comparison with the degradation product **22**.[15] Total synthesis of such antibiotics, however, must resort to an intermediate that allows to distinguish between the two carbonyl groups as well as the alcohol functions of **22**. Vinyl ether **23** ($R^1 \neq R^2$) might be suited for this purpose (Scheme 6). Its synthesis, based upon the methodology described in the previous section, is outlined in Scheme 7.




(+)-Trienomycin A, B, C, D, E
X = OH, Y = H

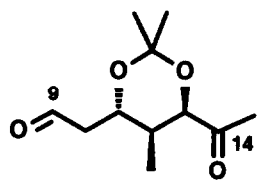
(+)-Mycotrienin II
X = Y = OH




(+)-Mycotrienin I

(+)-Ansatrienin $A_2$, $A_3$, $A_4$

Trienomycin A ⟶

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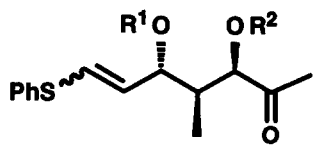
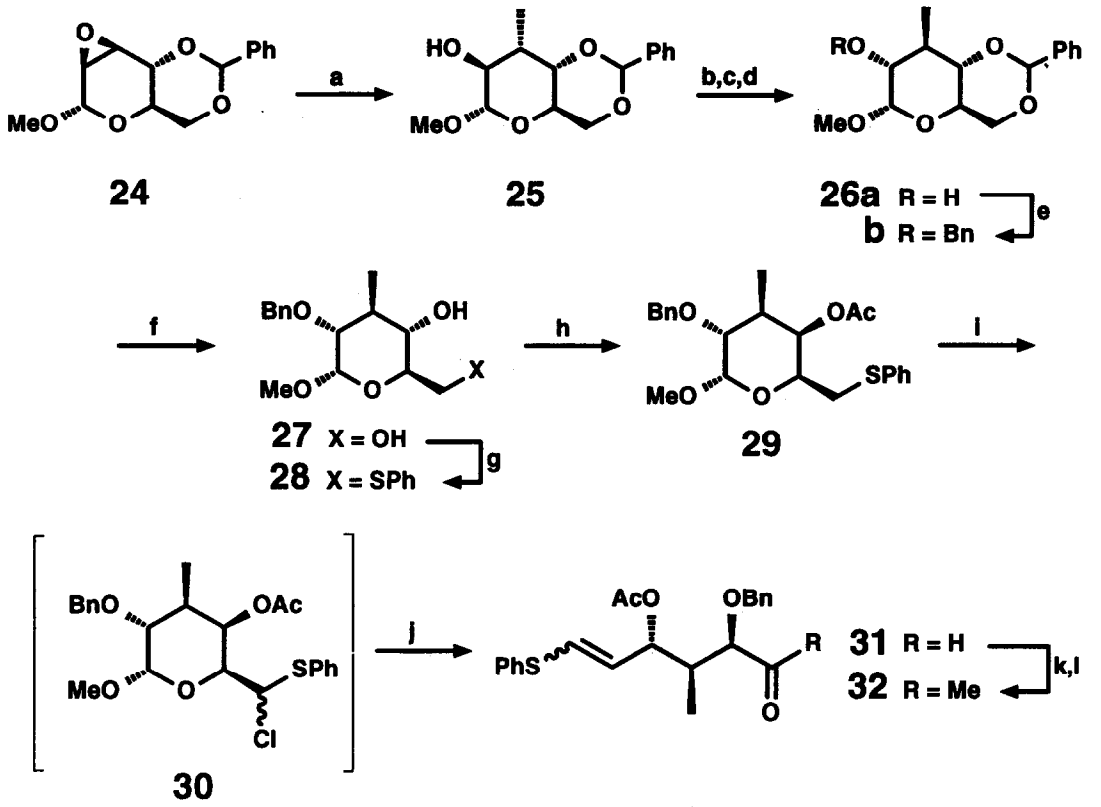



23

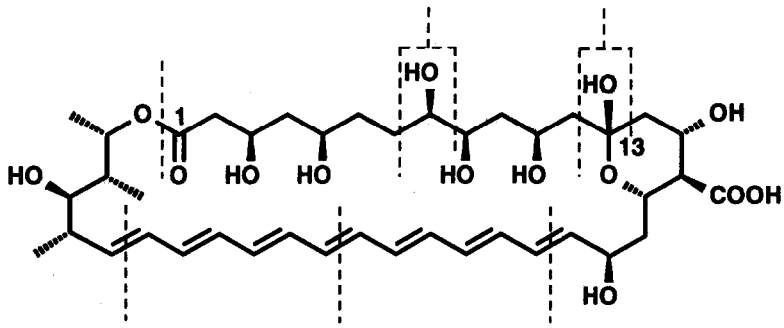
**Scheme 6.** Structures of the trienomycin-, mycotrienin- and ansatrienin antibiotics. R = differently N-acylated alanine derivatives. Degradation of trienomycin A.[15a]

Among a variety of reagents screened, MeMgCl gave best results in the regioselective trans-diaxial opening of the oxirane ring of methyl 2,3-anhydro-4,6-O-benzylidene-α-D-mannopyranoside **24**.[16] The configuration of the resulting alcohol **25** at C-2/C-3 was inverted following literature procedures via Swern oxidation, equilibration of the methyl group vicinal to the resulting ulose to the thermodynamically favourable equatorial orientation, and stereoselective reduction of the rigid bicyclic ketone.[17] This one-pot sequence afforded **26a** on a multigram scale. Following the necessary protecting group manipulation, diol **27**, on treatment with diphenyl disulfide/$Bu_3P$ gave 6-phenylthioether **28** selectively, ready for introduction of an acyl group at C-4 via nucleophilic substitution of the respective triflate.[18] Halogenation with NCS and ring-opening of the crude 6-chloro-6-phenylthiogalactopyranoside **30** with zinc/silver-graphite in DME proceeded smoothly. Chemoselective attack onto the aldehyde group of the 6-phenylthio-hex-5-enal **31** formed with $MeTi(O\text{-}iPr)_3$[19] and final oxidation of the resulting alcohol to the methylketone **32** afforded this synthon in 12 steps with an overall yield of 18% from **24**.

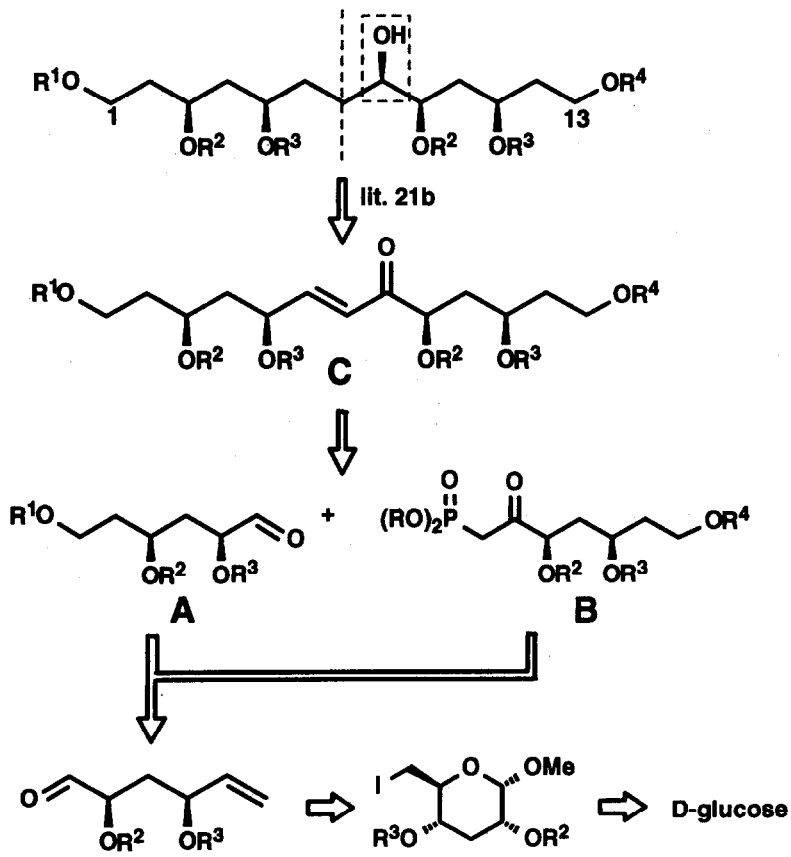



**Scheme 7.** Synthesis of the chiral core of the trienomycin- and mycotrienin antibiotics: (a) MeMgCl, $Et_2O$, 95%; (b) oxalyl chloride, DMSO, $Et_3N$, $CH_2Cl_2$; (c) $NEt_3$, DMF; (d) $NaBH_4$, 87% (over steps b-d); (e) KH, BnBr, THF, 78%; (f) p-TsOH.$H_2O$, MeOH, 92%; (g) PhSSPh, $Bu_3P$, pyridine, 83%; (h) (i) triflic anhydride, pyridine, $CH_2Cl_2$; (ii) $Bu_4N^+$ $AcO^-$, MeCN, 78%; (i) NCS, $CCl_4$; (j) Zn/Ag-graphite, DME, 66% (over steps i and j); (k) $MeTi(O\text{-}iPr)_3$, THF; (l) PCC, $CH_2Cl_2$, 72 % (over steps k and l).

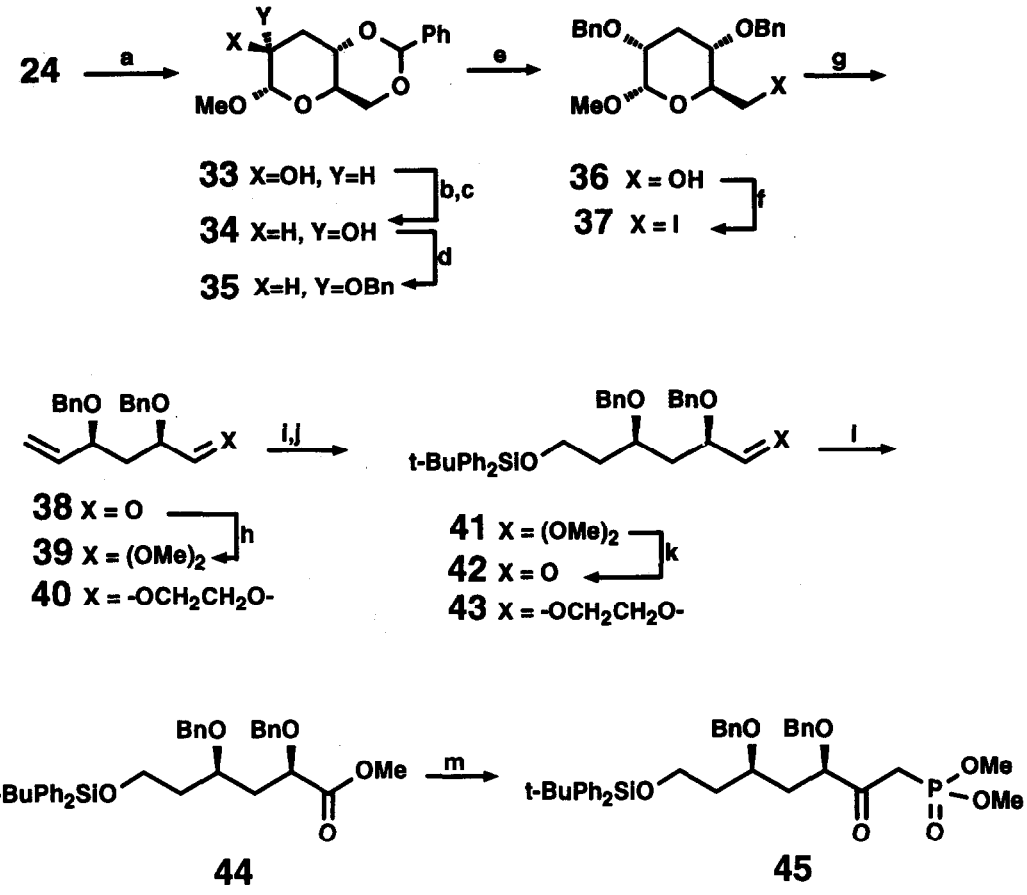
***The C1-C13 Fragment of Amphoteronolide B.*** The extensive work on the polyene macrolide amphotericin B,[20] a potent fungicide in clinical use produced by *Streptomyces nodosus*, has recently cumulated in a landmark total synthesis of this antibiotic.[21,22] In particular the polyhydroxylated C1(C2)-C12(C13) segment of its aglycon amphoteronolide B (Scheme 8), has been in the focus of preparative chemists.[23,24] The "hidden" $C_2$-symmetry of this target molecule (*c.f.* Scheme 9) makes convergent syntheses based on the use of both enantiomeric forms of the same starting material feasible. While one of Nicolaou's two approaches to this segment nicely executed this retrosynthetic analysis, preparing synthon **A** ($R^1$ = Bn, $R^2$,$R^3$ = $CMe_2$) from D-(+)-xylose and synthon **B** ($R^2$,$R^3$= Bn, $R^4$ = $SiMe_2$t-Bu) from L-(-)-xylose, respectively, in a linear manner,[21b] we felt that our enal transposition sequence (Scheme 2)[7] might also be useful in this context. As outlined in Scheme 9, we envisaged a convergent synthesis that allows the preparation of both halves **A** and **B** of the target molecule from the same precursor, *i.e.* from the inexpensive and readily available methyl α-D-glucopyranoside. By coupling the two sub-units to the enone **C** as shown in Scheme 9 this plan should coincide with Nicolaou's tactics[20d,21] except for the protecting groups employed.




**Scheme 8.** Amphoternolide B. The dotted lines indicate the strategic dissections of previous synthetic studies.[20]




**Scheme 9.** Retrosynthetic analysis for the synthesis of the C1-C13 segment of amphoteronolide B.

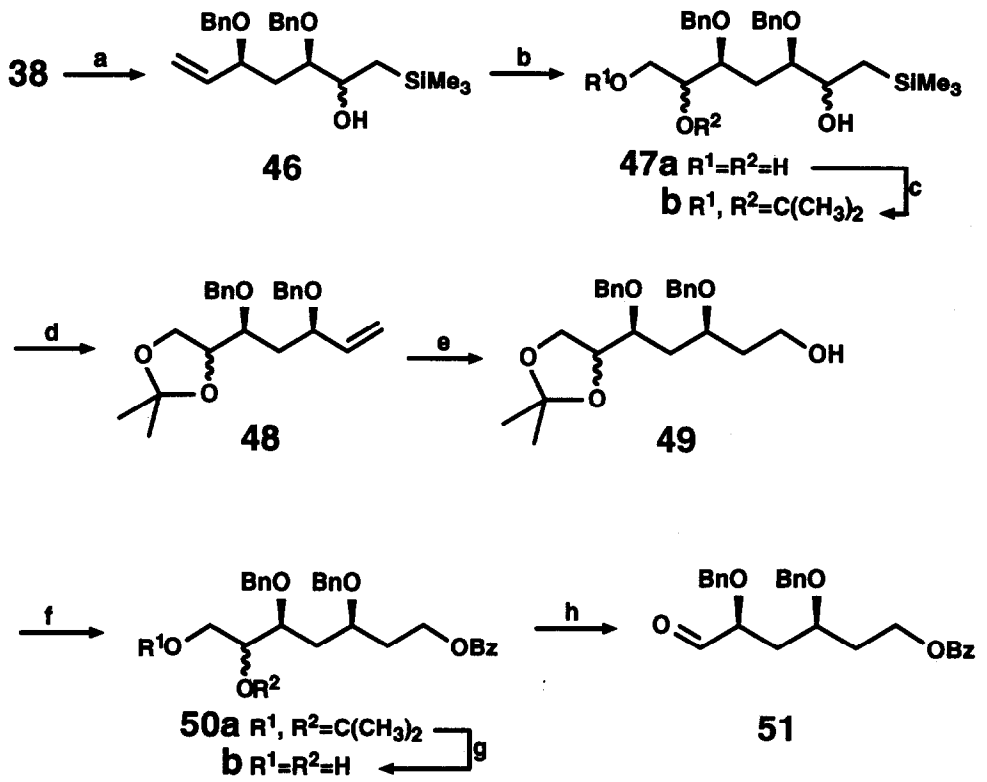



**Scheme 10.** The C7-C13 fragment of amphotericin B: (a) $LiAlH_4$, $Et_2O$, 90%; (b) oxalyl chloride, DMSO, $NEt_3$, $CH_2Cl_2$; (c) $NaBH_4$, $CH_2Cl_2/H_2O$, 93% (over both steps); (d) KH, BnBr, THF, 95%; (e) $BH_3.NMe_3$, $AlCl_3$, toluene, 66%; (f) $I_2$, $PPh_3$, imidazole, toluene, 88%; (g) Zn/Ag-graphite, THF, 86%; (h) $HC(OMe)_3$, p-TsOH, MeOH, 97%; (i) 9-BBN, $H_2O_2$; (j) t-$BuPh_2SiCl$, imidazole, DMF, 86% (both steps); (k) p-$TsOH.H_2O$, acetone, 95%; (l) PCC, MeOH, DMF, 68%; (m) $MeP(O)(OMe)_2$, n-BuLi, DME, 90%.

As for the trienomycin C9-C14 segment, anhydrosugar **24**[25] again served as starting material. Treating **24** with $LiAlH_4$ in diethyl ether introduced the necessary deoxyfunction, followed by oxidation/-reduction in order to establish the correct configuration at C-2 (**33**→**34**).[26] After O-benzylation (**34**→**35**) best achieved with KH as base, the 4,6-O-benzylidene acetal was reductively cleaved in a regioselective manner with $BH_3.NMe_3/AlCl_3$ in toluene[27] to dibenzyl ether **36**, thus liberating the primary alcohol at C-6. Exchange of -OH for iodine under standard conditions[6b,28] gave excellent yields of iodide **37**. Its zinc/silver-graphite[6-8] induced reductive cleavage proceeded almost instantaneously in good yield on a multigram scale. Thus, sufficient amounts of enal **38** were available, which constitutes the major synthon for both halves of the target molecule.

The C7-C13 subunit (Scheme 10) was obtained by hydroboration/oxidation of the aldehyde dimethylacetal **39** with 9-BBN/$H_2O_2$,[29] followed by silylation of the resulting primary alcohol group with

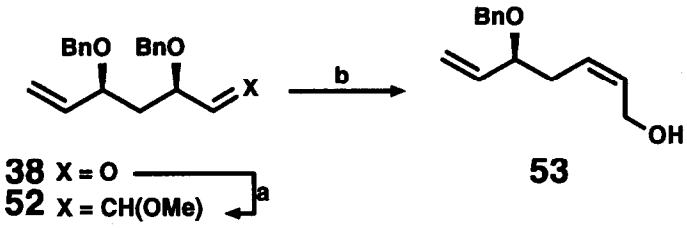
a slight excess of $tBuPh_2SiCl$ in DMF/imidazole.[30] After deprotection of the aldehyde function, compound **42** was oxidized to the methyl ester **44** using the PCC/MeOH/DMF reagent combination;[31] the latter could be converted to the ketophosphonate **45** upon treatment with lithio dimethyl methylphosphonate in THF at -78°C.[21b] It should be noted that masking aldehyde **38** as dimethylacetal **39** was essential, since on formation of the corresponding dioxolane derivative **40**, epimerization at the 2-position of the building block was observed. Furthermore attempted cleavage of the dioxolane group in **43** resulted in concomitant hydrolysis of the *tert*-butyldiphenylsilyl ether.




**Scheme 11.** Synthesis of the C1-C6 fragment of amphoteronolideB: (a) $TMSCH_2MgCl$, THF; (b) $OsO_4$ cat., NMNO, acetone, 88% (both steps); (c) 2,2-dimethoxypropane, p-TsOH, acetone, 87%; (d) $BF_3.Et_2O$ cat., $CH_2Cl_2$, 68%; (e) 9-BBN, $H_2O_2$, NaOH aq., THF, 93%; (f) PhCOCl, pyridine, DMAP cat., 89%; (g) p-TsOH.$H_2O$, THF/$H_2O$; (h) $NaIO_4$, $CH_2Cl_2/H_2O$, 78% (both steps).

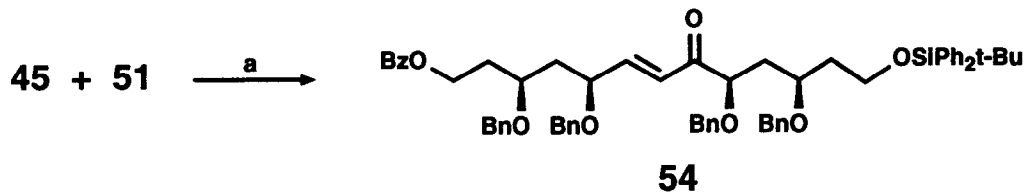
Aldehyde **51** as the coupling partner for the ketophosphonate **45** was prepared following closely the transposition sequence for enantiomerically pure hex-5-enals described recently (Scheme 11).[7] It avoids any *meso*-intermediates by a series of nucleophilic attack with $Me_3SiCH_2MgCl$ onto the carbonyl group of **38**, dihydroxylation (**46**→**47**) of the double-bond with $OsO_4$/N-methylmorpholine-N-oxide, acid-catalyzed Peterson elimination (**47**→**48**) and final periodide fission after setting free the terminal 1,2-diol group (**50b**→**51**). As in the model studies,[7] the protection of the diol **47a** formed in the $OsO_4$ catalyzed hydroxylation as acetonide **47b** proved advantageous avoiding any side reactions in the $BF_3.Et_2O$-induced

Peterson olefination step.[32] Furthermore, in this specific application the acetal was kept until the terminal hydroxy group had been introduced by hydroboration (**48**→**49**) and blocked as benzoate ester (**49**→**50a**). Since all transformations of this sequence proceeded without difficulty over several steps without isolation or separation of the intermediates (obtained as mixtures of diastereoisomers for compounds **46** - **50**) (*c.f.* experimental), the formal "transposition" of enal **38** to aldehyde **51** proceeded in 34% overall yield.




**Scheme 12.** Attempted approach to the C1-C6 fragment via Wittig reaction: (a) $Ph_3P$=CH(OMe), $Et_2O$, 70%; (b) $NaBH_3CN$, HCl, $Et_2O$, 65%.

An alternative approach to the C1-C6 unit (Scheme 12) aiming at simultaneous introduction of an oxygen function with C-C-bond formation, failed as the result of elimination of BnOH upon attempted acid-catalyzed hydrolysis of the enol ether **52** obtained by Wittig reaction of enal **38** with (MeO)CH=$PPh_3$.[33]




**Scheme 13.** Coupling of the C1-C6 with the C7-C13 fragment: (a) NaH, DME, 86%.

Reaction of the sodium anion of **45** with aldehyde **51** in DME gave 86% of the (E)-isomer of enone **54** as evident from the coupling constant $^3J$(*-CH=CHCO-*) = 15.7 Hz (Scheme 13). Although a different protecting group strategy was chosen, our synthesis (Scheme 9, $R^1$=Bz, $R^2$=$R^3$=Bn, $R^4$=$SiPh_2$t-Bu) meets Nicolaou's work (Scheme 9, $R^1$=Bn, $R^2$,$R^3$=$CMe_2$, $R^4$=$SiMe_2$t-Bu )[21] at this point. Starting from D-glucose, this approach turned out to be high yielding and distinctly shorter than previous ones. It therefore constitutes the basis for further work in progress in this laboratory.

## EXPERIMENTAL

**General.** Instrumentation used as described recently.[6] $[\alpha]_D$ values were invariably recorded in $CH_2Cl_2$ as solvent, NMR spectra in $CDCl_3$. MeMgCl, $TMSCH_2MgCl$ and $Bu_3P$ (techn. grade) were purchased from Aldrich and used as received. Molecular sieves 3Å and 4Å (powder, Union Carbide) were

activated by heating at 150°C under vacuum for 3 h, tetra-n-butylammonium acetate was dried overnight over $P_4O_{10}$ under vacuum in a desiccator. Anhydrous solvents were obtained by distillation under Ar from the drying agents given: THF and DME (potassium/benzophenone), toluene (sodium wire), $CCl_4$ ($P_4O_{10}$), $CH_2Cl_2$ ($CaH_2$), MeCN and pyridine (molecular sieves). KH was washed under argon with petrol ether (35-60°C) prior to use. Graphite powder (KS 5-44) supplied by Lonza AG, Switzerland was used for the preparation of the metal-graphite reagents. Substrates **8**,[34] **10**,[35] **12**,[36] **14**,[37] **16**[38] and **24**[25] were prepared according to literature procedures.

**Preparation of Phenylthioethers. General Procedure.-** To a stirred solution of the respective 6-O-unprotected sugar derivative (3.0 mmol) and diphenyl disulfide (3.6 mmol) in pyridine (6 mL) was added $Bu_3P$ (1.21 g, 6 mmol) via syringe under argon. The reaction mixture was stirred at room temperature until TLC showed complete conversion of the starting material. For work-up the solution was diluted with $CH_2Cl_2$ (70 mL), extracted with HCl (3N, 25 mL), the organic layer washed with sat. $NaHCO_3$ (15 mL) and water (15 mL), dried over $Na_2SO_4$ and evaporated. The crude residue was subjected to column chromatography using toluene (~300 mL) to elute excess PhSSPh, followed by the mixture of toluene/ethyl acetate as indicated for the individual compounds. Analytical and spectroscopic data are compiled below.

**Methyl 2,3,4-Tri-*O*-benzyl-6-*S*-phenyl-6-thio-α-D-glucopyranoside (9).-** Obtained after a reaction time of 5 h. Toluene/ethyl acetate (25/1) as eluent for flash chromatography. Colorless oil (86%); $[\alpha]_D^{23}$ = +50.3° (c 1.1); $^1$H-NMR: 7.17-7.38 (m, 20H); 5.02 and 4.85 (AB-system, 2H, J=11); 4.94 and 4.70 (AB-system, 2H, J=11); 4.81 and 4.62 (AB-system, 2H, J=11); 4.61 (d, 1H, J = 3.6); 4.01 (vt, 1H, J = 9.1); 3.88 (ddd, 1H, J = 9.5, 8.2, 2.3); 3.57 (dd, 1H, J = 9.1, 3.6); 3.43 (dd, 1H, J = 9.5, 9.1); 3.40 (s, 3H, -OMe); 3.36 (dd, 1H, J = 13.2, 2.3); 2.95 (dd, 1H, J = 13.2, 8.2); $^{13}$C-NMR: 138.97, 138.39, 137.18, 129.29, 129.09, 128.71, 128.48, 128.35, 128.22, 128.06, 127.89, 126.06, 98.17, 82.30, 81.05, 80.37, 76.01, 75.42, 73.59, 69.89, 55.41, 36.24.

**Methyl 2,3-Di-*O*-methyl-6-*S*-phenyl-6-thio-α-D-glucopyranoside (11).-** Work-up after a reaction time of 6h; Toluene/ethyl acetate (7/1) as eluent for column chromatography; colorless oil (98%); $[\alpha]_D^{23}$ = +131.3° (c 3.5); $^1$H-NMR: 7.13-7.40 (m, 5H); 4.84 (d, 1H, J = 3.4); 3.80 (dt, 1H, J = 8.7, 2.2); 3.62, 3.48, 3.41 (s, 3H each, -OMe); 3.52-3.35 (m, 3H); 3.24 (dd, 1H, J = 9.1, 3.4); 3.05 (dd, 1H, J = 13.8, 8.7); 2.93 (bs, 1H, -OH); $^{13}$C-NMR: 137.68, 129.09, 129.03, 126.02, 97.48, 83.03, 82.15, 73.15, 70.25, 61.31, 58.55, 55.34, 36.05.

**1,2;3,4-Di-*O*-isopropylidene-6-*S*-phenyl-6-thio-α-D-galactopyranoside (13).-** Reaction time for thioether formation was 12 h; toluene/ethyl acetate (25/1) as eluent for flash chromatography; colorless oil (86%); $[\alpha]_D^{23}$ = -91.2° (c 1.2) (lit.[13b] -39.9 (c 1.4, $CHCl_3$)); $^1$H-NMR: 7.13-7.41 (m, 5H); 5.53 (d, 1H, J = 5.0); 4.60 and 4.38 (dAB-system, 2H, J = 8, 2.3, 1.7); 4.28 (dd, 1H, J = 5, 2.3); 3.84 (dd, 1H, J = 7, 1.7); 3.17 (d, 2H, J = 7); 1.46, 1.35, 1.27, 1.23 (s, 3H each, -Me); $^{13}$C-NMR: 137.89, 129.70, 129.10, 126.31, 109.46, 108.72, 96.87, 71.49, 71.12, 70.80, 66.46, 33.47, 26.19, 25.83, 25.09, 24.66.

**2,3-*O*-Isopropylidene-5-*S*-phenyl-5-thio-D-ribono-1,4-lactone (15).-** TLC showed quantitative conversion to the thioether after 5 h reaction time; in this specific case toluene was the only eluent for flash chromatography; colorless oil (94%); $[\alpha]_D^{23}$ = -12.0° (c 4.0); $^1$H-NMR: 7.14-7.34 (m, 5H); 4.85 (d, 1H, J = 6.0); 4.67 (dd, 1H, J = 6.3, 3.7); 4.59 (d, 1H, J = 6); 3.22 and 3.10 (dAB-system, 2H, J = 14.6, 6.3); 1.37, 1.27 (s, 3H each, -Me); $^{13}$C-NMR: 173.34, 134.24, 130.33, 129.55, 127.32, 113.53, 81.42, 78.69, 75.04, 37.06, 25.38, 24.47.

**Methyl 2,3-*O*-Isopropylidene-5-*S*-phenyl-5-thio-α-D-lyxofuranoside (17).-** Performed on a 12 mmol scale with **16** (2.5 g, 12.24 mmol) and PhSSPh (3.20 g, 14.69 mmol) and $PBu_3$ (4.95 g, 24.48 mmol) in pyridine (10 mL). The conversion was complete after 6 h at room temperature. Work-up as described above with hexane/ethyl acetate (4/1) as eluent afforded the product as colorless oil (3.16 g, 87%). $[\alpha]_D^{20}$ = +18.9 (c 1.5); $^1$H-NMR: 7.12-7.43 (m, 5H); 4.88 (s, 1H); 4.70 (dd, 1H, J = 5.8, 3.5); 4.54 (d, 1H, J = 5.8); 4.06 (dt, 1H, J = 6.9, 3.5); 3.29 (s, 3H); 325 (d, 2H, J = 6.9); 1.46, 1.32 (s, 3H each). $^{13}$C-NMR: 135.61, 129.21, 128.58, 125.90, 112.26, 106.77, 84.68, 79.42, 78.10, 54.20, 31.64, 25.76, 24.61..

**Methyl 4-*O*-Acetyl-2,3-di-O-methyl-6-*S*-phenyl-6-thio-α-D-galactopyranoside (19).-** To a stirred solution of compound **11** (2.0 g, 6.36 mmol) in $CH_2Cl_2$ (10 mL) and pyridine (2 mL) under argon was added triflic anhydride (3.58 g, 12.72 mmol) at 0°C. When TLC showed complete conversion of the substrate (20 min) the reaction was quenched with HCl (0.1N, 10 mL), the aqueous layer extraced with $CH_2Cl_2$ (30 mL) in three portions, the combined organic phases washed with $NaHCO_3$ (10 mL), dried over $Na_2SO_4$ and evaporated. The crude triflate was dissolved in acetonitrile (10 mL) and treated with thoroughly dried $Bu_4NOAc$ (4.00g, 13.26 mmol) at 0°→20°C for 60 min under argon. After evaporation of the solvent the residue was purified by column chromatography using toluene/ethyl acetate (7/1) as eluent affording **19** as colorless oil (2.57 g, 80%); $[\alpha]_D^{23}$ = +108.8° (c 2.5); $^1$H-NMR: 7.15-7.37 (m, 5H); 5.50 (d, 1H, J = 2.8); 4.90 (d, 1H, J = 3.1); 3.94 (dd, 1H, J = 8.0, 5.2); 3.57 and 3.52 (dAB-system, 2H, J = 9.8); 3.50, 3.40, 3.39 (s, 3H each, -OMe); 3.06 and 2.97 (dAB-system, 2H, J(AB) = 13.9); 2.15 (s, 3H, -OAc); $^{13}$C-NMR: 170.49, 136.13, 129.73, 129.21, 126.59, 98.29, 78.16, 77.42, 68.81, 68.15, 59.24, 57.98, 55.55, 35.01, 20.94.

**Reductive Ring Opening of ω-Chloro-ω-phenylthioglycosides with Zn/Ag-Graphite. Representative Procedure.-** NCS (0.764 mg, 5.72 mmol) was added to a solution of compound **19** (1.70 g, 4.77 mmol) in $CCl_4$ (11 mL) under Ar. After stirring for 2 h at room temperature, the reaction mixture was filtered under Ar, the solvent removed *in vacuo* and the residue co-evaporated twice with DME (5 mL each). The crude chlorothioether was dissolved in DME (2 mL) and added to a freshly prepared suspension of Zn/Ag-graphite (15 mmol)[6] in DME (35 mL) at 40°C. After 10 min TLC showed complete conversion of the substrate. The mixture was filtered, the graphite washed with DME (40 mL) in several portions, the combined filtrates evaporated and the residue purified by flash chromatography using toluene/ethyl acetate (7/1) as eluent. Thus, compound **20** (905 mg, 64%) (mixture of the (E)- and (Z)-isomer, (E)/(Z) = 2.5/1) was obtained as colorless oil. $[\alpha]_D^{20}$ = +56.5° (c 1.0); (E)-isomer (resolved signals): $^1$H-NMR: 9.80 (d, 1H, J=1.3); 6.60 (d, 1H, J=14.7); 5.72 (dd, 1H, J = 14.7); 5.53 (dd, 1H, J = 8.0, 5.8); 3.49, 3.39 (s, 3H each); 2.07(s, 3H); $^{13}$C-NMR: 203.05, 169.50, 85.37, 82.55, 73.09, 70.41, 60.61, 59.78, 21.27. (Z)-isomer (resolved signals): $^1$H-NMR: 6.51 (d, 1H, J = 9.6); 5.94 (dd, 1H, J = 8.2, 5.2); 5.79 (dd, 1H, J = 9.6, 8.2); 3.52, 3.46 (s, 3H each); 2.09 (s, 3H); $^{13}$C-NMR: 202.80, 85.57, 82.32, 60.35, 59.42, 21.14.

**5-Deoxy-2,3,4-tri-*O*-benzyl-6-*S*-phenyl-6-thio-D-*xylo*-hex-5-enose (18).-** A mixture of the (E)- and (Z)-isomer ((E):(Z) = 2.5:1) was obtained according to the representative procedure described above as colorless oil (416 mg, 67%) from substrate **9** (660 mg, 1.19 mmol) using toluene/ethyl acetate (25/1) as eluent in flash chromatography. $[\alpha]_D^{23}$ = +23° (c 1.5); (E)-isomer (resolved signals): $^1$H-NMR: 9.73 (s, 1H); 6.44 (d, 1H, J = 15.1); 5.77 (dd, 1H, J = 15.1, 7.7); $^{13}$C-NMR: 201.43, 82.66, 81.90, 79.50, 74.66, 73.55, 71.38. (Z)-isomer (resolved signals): $^1$H-NMR: 6.56 (d, 1H, J = 9.6), 5.95 (dd, 1H, J = 9.6, 7.5); $^{13}$C-NMR (resolved signals): 82.84, 81.41, 75.46, 71.64.

**4-Deoxy-2,3-O-isopropylidene-5-*S*-phenyl-5-thio-L-*erythro*-pent-4-enose (21).-** Obtained as colorless oil (977 mg, 73%) upon reaction of substrate 17 (1.50 g, 5.06 mmol) according to the procedure given above with hexane/ethyl acetate (10/1) as eluent for column chromatography. *(E):(Z)* = 4.8 : 1; $[\alpha]_D^{20}$ = +33.2 (c 1.2); (E)-isomer (resolved signals): $^1$H-NMR: 9.54 (d, 1H, J = 3); 7.22-7.40 (m, 5H); 6.62 (d, 1H, J = 15.3); 5.52 (dd, 1H, J = 15.3, 7.4); 4.90 (vt, 1H, J = 7.4); 4.39 (dd, 1H, J = 7.4, 3); 1.60, 1.43 (s, 3H each); $^{13}$C-NMR: 200.17, 122.31, 111.08, 82.11, 78.40, 27.26, 25.19. (Z)-isomer (resolved signals): $^1$H-NMR: 9.59 (d, 1H, J = 3); 6.52 (d, 1H, 9.8); 5.71 (dd, 1H, J = 9.8, 8); 5.32 (vt, 1H, J = 7.4); 4.50 (dd, 1H, J = 7.4, 3); 1.65, 1.47 (s, 3H each); $^{13}$C-NMR: 199.62, 123.73, 111.27, 81.75, 27.22.

**Methyl 4,6-O-Benzylidene-3-deoxy-3-C-methyl-α-D-altropyranoside (25).-** To a suspension of compound **24** (10 g, 37.8 mmol) in diethyl ether (550 mL) was added MeMgCl (190 mL, 20% solution in THF, 567.5 mmol). The mixture was refluxed under nitrogen for 7 d, poured into $NH_4Cl$ (3N, 600 mL) and the aqueous phase extracted with ether (500 mL) in several portions. The combined organic layers were dried ($Na_2SO_4$), evaporated and the crude residue purified by column chromatography with toluene/ethyl acetate (5/1) as eluent. This afforded the product (10.08 g, 95%) as white crystals. mp = 113-115°C (lit.[16] 115°C) $[\alpha]_D^{20}$ = +97.6° (c 1.2) [lit. [16] +120° (c 1.7, $CHCl_3$)]. $^1$H-NMR: 7.21-7.55 (m, 5H); 5.61 (s, 1H); 4.60 (s, 1H); 4.30 (dd, 1H, J = 4.7, J = 10.3); 4.03 and 4.07 (dAB-system, 2H, J = 3.3, J = 4.7, J = 12); 3.80 (m, 2H); 3.41 (s, 3H); 2.12 (m, 1H); 1.73 (bs, 1H, -OH); 1.23 (d, 3H, J = 7.4). $^{13}$C-NMR: 137.91, 129.26 128.49, 126.54, 126.46, 102.45, 102.16, 76.48, 73.08, 69.62, 58.91, 55.37, 37.33, 10.94.

**Methyl 4,6-O-Benzylidene-3-deoxy-3-C-methyl-α-D-glucopyranoside (26a).-** To a solution of oxalyl chloride (5.2 g, 41.3 mmol) in $CH_2Cl_2$ (40 mL) under Ar was slowly added DMSO (4.00g, 50.7 mmol) at -78°C. After stirring for 15 min, a solution of compound **25** (10.1 g, 36.0 mmol) in $CH_2Cl_2$ (10 mL) was added dropwise at the same temperature, followed by $NEt_3$ (32.7 g, 323 mmol) after an additional stirring of 15 min. The reaction was allowed to warm to room temperature and quenched with water (100 mL). The aqueous phase was extracted with $CH_2Cl_2$ (100 mL) in three portions, the combined organic layers dried ($Na_2SO_4$) and evaporated. The crude ulose thus obtained was dissolved in DMF (150 mL), treated with $NEt_3$ (5 ml) and stirred for 3 days in order to equilibrate the methyl substituent to the equatorial position. After addition of water (150 mL) conventional extractive work-up with $CH_2Cl_2$ (200 mL) gave the crude methyl 4,6-O-benzylidene-3-deoxy-3-C-methyl-α-D-arabino-hex-2-ulopyranoside,[17] which was reduced with $NaBH_4$ without further purification to afford the title compound. This was done in a biphasic system of a solution of the crude ulose in $CH_2Cl_2$ (35 mL) and water (35 mL) by adding $NaBH_4$ (2.1 g, 55.5 mmol) in several portions under vigorous stirring. After separating, drying ($Na_2SO_4$) and evaporating of the organic layer the residue was subjected to column chromatography using toluene/ethyl acetate (15/1) as eluent. This afforded compound **26a** in 8.70 g (87% overall yield from **25**) as a syrup, that crystallized upon standing at room temperature. mp = 150-152°C (lit.[17] 150.5-151.5°C) $[\alpha]_D^{23}$ = +92.1° (c 1.3) [lit. [17] +94° (c 1.04, $CHCl_3$)]; $^1$H-NMR: 7.33-7.52 (m, 5H); 5.51 (s, 1H); 4.69 (d, 1H, J = 3.6); 4.27 (dd, 1H, J = 4.2, J = 9.4); 3.74 (ddd, 1H, J = J = 9.6); 3.69 (dd, 1H); 3.46 (s, 3H); 3.35 (dd, 1H, J = 7.3); 3.16 (dd, 1H, J = 9.6); 2.1 (bs, 1H, -OH); 2.02 (m, 1H); 1.19 (d, 3H, J = 6). $^{13}$C-NMR: 137.88, 129.07, 128.64, 128.39, 128.00, 126.31; 101.73; 99.48; 81.60, 73.53, 69.44, 63.92; 55.47; 38.28; 13.11.

**Methyl 2-O-Benzyl-4,6-O-benzylidene-3-deoxy-3-C-methyl-α-D-glucopyranoside (26b).**- To a solution of **26a** (7.04g, 25.1 mmol), benzyl bromide (8.50g, 49.7 mmol) and a catalytic amount of tetra-n-butylammonium iodide (~0.1g) in THF (70 mL) under argon was added KH (1.20 g, 30 mmol) in several portions with good mechanical stirring. After 3 h at room temperature, i-PrOH (5 mL) was slowly added carefully surveying the evolution of gas, followed by addition of water (30 mL). Standard extractive work-up with $CH_2Cl_2$ (200 mL) and purification of the crude product by column chromatography (toluene/ethyl acetate = 25/1) afforded the product as syrup (7.02 g, 78%). mp= 96-98°C. $[\alpha]_D^{23}$ = + 63.8° (c 5.0); $^1$H-NMR: 7.34-7.56 (m, 10H); 5.52 (s, 1H); 4.68 (d, 1H, J = 3.3); 4.67 (s, 2H, -$CH_2$Ph); 4.29 (dd, 1H, J = 4.9, J = 10.2); 3.82 (ddd, 1H, J = J = 10); 3.69 (dd, 1H); 3.46 (s, 3H); 3.25 (dd, 1H, J = 10.5); 3.18 (dd, 1H, H-4, J = J = 10); 2.23-2.40 (m, 1H); 1.20 (d, 3H, J = 6.5). $^{13}$C-NMR: 138.28, 137.86, 129.03, 128.58, 128.35, 128.19, 128.05, 126.28; 101.76; 97.72; 82.09, 80.34, 72.64, 69.47, 63.66; 55.30; 35.99; 13.26.

**Methyl 2-O-Benzyl-3-deoxy-3-C-methyl-α-D-glucopyranoside (27).**- Stirring of a solution of **26b** (6.05g, 16.3 mmol) in MeOH (100 mL) with a catalytic amount of p-toluenesulfonic acid monohydrate (~0.3g) overnight at room temperature leads to clean deprotection of the 4,6-O-benzylidene acetal. For work-up the solution was neutralized with $Na_2CO_3$, filtered and the solvent removed *in vacuo*. Purification of the residue by flash chromatography (toluene/ethyl acetate = 1:1) gave **27** as a white crystalline compound (4.38 g, 92 %). mp = 118-120°C; $[\alpha]_D^{23}$ = +101.2° (c 1.8). $^1$H-NMR: 7.28-7.37 (m, 5H); 4.62 (d, 1H, J = 3.3); 4.61 (s, 2H); 3.79 (m, 2H); 3.53 (m, 1H); 3.39 (s, 3H); 3.23 (m, 1H); 3.10 (dd, 1H, J = 10.5, 3.3); 2.79 (d, 1H, -OH); 2.49 (bt, 1H, -OH); 2.02-2.07 (m, 1H); $^{13}$C-NMR: 136.41, 129.25, 128.64, 128.44, 128.25, 128.09; 97.14; 79.73, 72.64, 71.88, 63.10; 55.32; 38.32; 14.06.

**Methyl 2-*O*-Benzyl-3-deoxy-3-*C*-methyl-6-*S*-phenyl-6-thio-α-D-glucopyranoside (28).**- Prepared according to the general procedure outlined above using **27** (1.79g, 6.34 mmol) as substrate. After a reaction time of 3 h and the work-up as described for the model substrates, the title compound was obtained as colorless oil (1.98 g, 83%). $[\alpha]_D^{23}$ = +114.9° (c 3.7); $^1$H-NMR: 7.16-7.42 (m, 10H), 4.66 (d, 1H, J = 3.3); 4.62 (s, 2H); 3.73 (dt, 1H, J = 7.7, 2.6); 3.47 (dd, 1H, J = 13.3, 2.6); 3.40 (s, 3H, -OMe); 3.02-3.17 (m, 3H); 2.09 (bs, 1H, -OH); 1.94-2.03 (m, 1H); 1.15 (d, 3H, J = 6.5); $^{13}$C-NMR: 138.34, 137.05, 129.16, 129.06, 128.58, 128.40, 128.16, 128.03, 126.09, 96.91, 79.60, 74.58, 72.51, 71.25, 55.18, 38.68, 36.45, 14.06.

**Methyl 4-*O*-Acetyl-2-*O*-benzyl-3-deoxy-3-*C*-methyl-6-*S*-phenyl-6-thio-α-D-galactopyranoside (29).**- To a stirred solution of compound **28** (1.80 g, 4.81 mmol) in $CH_2Cl_2$ (15 mL) and pyridine (2 mL) under Ar was added triflic anhydride (2.94 g, 10.42 mmol) at 0°C with good stirring. After 30 min the reaction was diluted with $CH_2Cl_2$ (50 mL), quenched with HCl (1N, 20 mL), the aqueous layer extracted with $CH_2Cl_2$ (30 mL) in three portions, the combined organic phases washed with $NaHCO_3$ and water (10 ml each), dried over $Na_2SO_4$ and evaporated. The crude triflate was dissolved in acetonitrile (15 mL) and treated with thoroughly dried $Bu_4NOAc$ (3.14 g, 10.42 mmol) at 0°C under Ar for 30 min. Evaporation of the solvent followed by column chromatography (toluene/ethyl acetate = 25/1) afforded the pure title compound as pale-yellow oil (1.56g, 78%). $[\alpha]_D^{23}$ = +91.0° (c 1.1); $^1$H-NMR: 7.18-7.37 (m, 10H); 5.19 (d, 1H, J = 1.8); 4.73 (d, 1H, J = 3.4); 4.60 (s, 2H); 4.02 (vt, 1H, J = 6.6); 3.48 (dd, 1H, J = 11, 3.4); 3.39 (s, 3H, -OMe); 2.95 (d, 2H, J = 6.6); 2.31 (ddq, 1H, J = 11, 6.9, 1.8); 2.13 (s, 3H); 0.98 (d, 3H, J = 6.9); $^{13}$C-NMR: 170.89, 138.51, 129.74, 129.22, 128.61, 128.45, 128.13, 128.06, 126.54, 97.72, 76.85, 73.52, 72.67, 68.95, 55.50, 35.34, 34.25, 20.89, 13.65.

**4-*O*-Acetyl-2-*O*-benzyl-3,5-dideoxy-3-*C*-methyl-6-*S*-phenyl-6-thio-L-*arabino*-hex-5-enose (31).**- Prepared according to the representative procedure given for chlorothioether formation and -fragmentation using **29** (1.30 g, 3.12 mmol), NCS (500 mg, 3.75 mmol) and Zn/Ag-graphite (15 mmol). After flash chromatography with toluene/ethyl acetate (25/1) enal **31** was obtained as mixture of the (E)- and (Z)-isomer ((E):(Z) = 2:1) as pale yellow oil (792 mg, 66%). $[\alpha]_D^{23}$ = +23.8° (c 8.2); (E)-isomer (resolved signals): $^1$H-NMR: 9.73 (s, 1H); 6.64 (d, 1H, J = 15.1); 5.60 (dd, 1H, J = 15.1, 8.3); 5.28 (dd, 1H, J = 8.3); 3.93 (d, 1H, J = 2.5); 1.92 (s, 3H); 0.94 (d, 3H); $^{13}$C-NMR: 203.79, 169.61, 82.54, 75.01, 73.03, 72.46, 38.85, 21.11, 10.63. (Z)-isomer (resolved signals): $^1$H-NMR: 9.76 (s, 1H); 6.50 (d, 1H, J = 9.0); 3.99 (d, 1H, J = 1.8); 1.94 (s, 3H); 1.01 (d, 3H); $^{13}$C-NMR: 203.70, 169.46, 20.92, 10.37.

**5(*R*)-Acetoxy-3(*R*)-benzyloxy-4(*R*)-methyl-7-phenylthio-hept-6-en-2-one (32).**- To a solution of enal **31** (250 mg, 0.65 mmol) in THF (3 mL) under Ar was added methyl tris(isopropoxy)titanium (312 mg, 1.3 mmol)[19] in THF (2 mL) at -20°C. After stirring for 3 h at -20°C and another 60 min at ambient temperature the mixture was quenched with HCl (5N, 10 mL), extracted with ethyl acetate (50 mL) in three portions, the organic layers washed with $NaHCO_3$ and brine (10 mL each), dried ($Na_2SO_4$) and evaporated. For analytical purposes a 50 mg fraction of the crude material was purified by flash chromatography with toluene/ethyl acetate (25/1) as eluent, affording an almost pure fraction of one isomer of the diastereomeric mixture obtained in the reaction with the following spectral parameters: $[\alpha]_D^{23}$ = +25.4° (c 0.35); $^1$H-NMR: 7.26-7.49 (m, 10H); 6.56 (d, 1H, J = 15.1); 5.66 (dd, 1H, J = 15.1, 8.1); 5.28 (dd, 1H, J = 8.5); 4.60 and 4.52 (AB-system, 2H, J = 11.1); 4.00-4.06 (m, 1H); 3.40 (dd, 1H, J = 5.5, 2.9); 2.06 (s, 3H); 2.02-2.18 (m, 1H); 1.93 (bs, 1H, -OH); 1.27 (d, 3H, J = 6.2); 1.01 (d, 3H, J = 6.9); $^{13}$C-NMR: 170.31, 138.57, 130.46, 129.84, 129.45, 129.35, 128.93, 128.71, 128.44, 128.19, 128.00,

127.44, 127.40, 81.71, 76.59, 73.94, 68.27, 38.13, 21.57, 19.37, 10.95.

The crude alcohol was dissolved in $CH_2Cl_2$ (2 mL), PCC (323 mg, 1.50 mmol) and molecular sieves 3Å (100 mg) were added, and the mixture stirred for 1.5 h at room temperature. After addition of diethyl ether (20 mL) the precipitated chromium salts were filtered off, the filtrate was evaporated and the residue subjected to column chromatography with toluene/ethyl acetate (15/1) as eluent. This gave the title compound as colorless oil (151 mg, 58 % over both steps) as a mixture of the (E)- and (Z)-isomer (*(E):(Z)* = 1.5:1). $[\alpha]_D^{23}$ = +27° (c 0.3); *(E)*-isomer: $^1$H-NMR: 7.18-7.42 (m, 10H); 6.59 (d, 1H, J = 15.0); 5.53-5.62 (m, 1H); 5.21 (dd, 1H, J = 9.0); 4.66 and 4.40 (AB-system, 2H, J = 11.8); 4.00 (d, 1H, J = 3.4); 2.25-2.37 (m, 1H); 2.23 (s, 3H); 1.95 (s, 3H); 0.96 (d, 3H, J = 7.2); $^{13}$C-NMR: 211.07, 169.86, 137.60, 130.83, 130.46, 130.26, 129.45, 129.29, 128.74, 128.44, 128.25, 128.19, 128.06, 127.44, 127.35, 127.21, 84.06, 75.41, 73.37, 72.67, 53.62, 39.98, 26.97, 21.34, 10.86. *(Z)*-isomer (resolved signals): $^1$H-NMR: 6.49 (dd, 1H, J = 6.8, 1.8); 5.29 (m, 1H); 4.62 and 4.33 (AB-system, 2H, J = 11.8); 3.93 (d, 1H, J = 3.6); 2.21 (s, 3H); 1.94 (s, 3H); 0.89 (d, 3H, J = 6.8); $^{13}$C-NMR: 210.89, 169.73, 137.46, 84.15, 40.06, 27.12, 21.11, 10.51.

**Methyl 4,6-O-Benzylidene-3-deoxy-α-D-*arabino*-hexopyranoside (33).-** To a solution of the anhydro sugar **24** (15.00 g, 56.8 mmol) in diethyl ether (500 mL) was added $LiAlH_4$ (3.00 g, 79.0 mmol) in several portions at 0°C. After the addition was complete, the mixture was refluxed for 12 h under nitrogen, cooled to room temperature and quenched with a saturated solution of $MgSO_4$ (12 mL) carefully controling the exothermic reaction. After filtration through a pad of celite, the remaining salts were extracted with boiling ethyl acetate (200 mL each), the combined organic layers evaporated and the residue chromatographed with toluene/ethyl acetate (15/1) as eluent. Thus, the product was obtained as white crystals (13.6 g, 90%). mp=117-120°C (lit[39] 111-112°C); $^1$H-NMR: 7.30-7.53 (m, 5H); 5.60 (s, 1H); 4.57 (s, 1H); 4.27 (dd, 1H, J = 2.8, J = 8.7); 3.99 (m, 2H); 3.85 (m, 2H); 3.44 (s, 3H); 2.38 (bs, 1H, -OH); 2.05-2.15 (m, 2H). $^{13}$C-NMR: 137.67, 129.09, 128.32, 126.28, 102.12, 100.86, 73.94, 69.32, 68.24, 65.08, 54.79, 32.01.

**Methyl 4,6-O-Benzylidene-3-deoxy-α-D-*ribo*-hexopyranoside (34).-** To a solution of oxalyl chloride (5.60 g, 64.6 mmol) in $CH_2Cl_2$ (100 mL) was added DMSO (5.60 mL, 79.0 mmol) at -70°C under Ar. After stirring for 15 min a solution of **33** (15.00 g, 56.3 mmol) in $CH_2Cl_2$ (180 mL) was added dropwise. When the addition was complete, the reaction mixture was stirred for 15 min at the same temperature, and $NEt_3$ (70 mL) was slowly added. The mixture was allowed to warm to room temperature, quenched with water (100 mL) followed by addition of $NaBH_4$ (3.50 g, 92.5 mmol) in several portions to the two-phase system with vigorous stirring. After 2 h the aqueous phase was twice extraced with $CH_2Cl_2$ (50 mL each), the combined organic layers dried ($Na_2SO_4$) and the solvent removed *in vacuo*. Flash chromatography using toluene/ethyl acetate (15/1) leads to analytically pure **34** (13.95 g, 93%). mp= 186-188°C, (lit.[26b] 190-191°C). $^1$H-NMR: 7.35-7.61 (m, 5H); 5.54 (s, 1H); 4.70 (d, 1H, J = 3.7); 4.29 (vq, 1H, J = 10.7); 3.80 (dt, 1H); 3.73 (m, 2H); 3.56 (m, 1H); 3.49 (s, 3H); 2.32 (dt, 1H, J = 11.3); 2.16 (bs, 1H, -OH); 1.88 (vq, 1H). $^{13}$C-NMR: 137.58, 129.19, 128.42, 126.35, 101.86, 99.29, 76.48, 69.48, 67.76, 64.09, 55.39, 33.87.

**Methyl 2-O-Benzyl-4,6-O-benzylidene-3-deoxy-α-D-*ribo*-hexopyranoside (35).** To a suspension of KH (2.49 g, 61.8 mmol) in THF (80 mL) was added dropwise a solution of **34** (15.00g, 56.3 mmol) in THF (100 mL) at 0°C under Ar. After 30 min at room temperature, benzyl bromide (11.0 mL, 92.50 mmol) was slowly added and stirring continued for another 30 min. For work-up i-PrOH (50 mL) and water (50 mL) were successively added carefully monitoring the vigorous reaction. After extraction with $CH_2Cl_2$ (200 mL) in several portions, the organic phase was dried ($Na_2SO_4$), the solvent evaporated and the residue subjected to column chromatography using toluene/ethyl acetate (25/1) as eluent. Thus, the product was obtained as white, crystalline solid (19.07 g, 95%). mp=90-92°C (lit.[40] 95.5-96.5°C). $[\alpha]_D^{20}$ = +36.6° (c 3.5) [lit.[40] +19.2° (c 1.0, $CHCl_3$)]. $^1$H-NMR: 7.31-7.57 (m, 10H); 5.54 (s, 1H); 4.75 (d, 1H, J = 3.7); 4.64 and 4.70 (AB-system, 2H, -$CH_2$Ph, J = 13.9); 4.30 (dd, 1H, J = 4.1); 3.83 (ddd, 1H, J = 9.9, 9.5, 4.5); 3.71 (t, 1H, J = 9.5); 3.65 (m, 1H); 3.52 (ddd, 1H, J = 12, 9.9, 4.5); 3.50 (s, 3H, -OMe), 2.30 (dt, 1H, J = 11.6); 2.13 (dd, 1H, J = 12, 4.5); $^{13}$C-NMR: 138.12, 137.64, 129.12, 128.58, 128.37, 127.98, 127.93, 126.34, 101.84, 98.15, 76.85, 74.17, 71.15, 69.51, 64.11, 55.17, 30.30.

**Methyl 2,4-Di-O-benzyl-3-deoxy-α-D-*ribo*-hexopyranoside (36).-** $BH_3.NMe_3$ (2.50 g, 35.3 mmol) and molecular sieves 4Å (powder, 2.5 g) were suspended in toluene (30 mL), stirred for 30 min at room temperature under Ar, followed by slow addition of $AlCl_3$ (3.00 g, 22.5 mmol). After addition of **35** (2.00 g, 5.60 mmol) the mixture was allowed to react for 10 min, quenched with $H_2SO_4$ (2N, 7 mL) with vigorous stirring for another 10 min, filtered, the aqueous phase washed with $NaHCO_3$ (10 mL) and neutralized with $NEt_3$. After drying ($Na_2SO_4$) and removal of the solvent *in vacuo* chromatography using toluene/ethyl acetate (20/1) as eluent afforded the title compound as colorless oil (1.21 g, 66 %). $[\alpha]_D^{23}$ = +71.6° (c 3.3). $^1$H-NMR: 7.25-7.37 (m, 10H); 4.67 (d, 1H, J = 3.2); 4.60 and 4.64 (AB-system, 2H, J = 12); 4.47 and 4.63 (AB-system, 2H, J = 11.5); 3.71-3.83 (m, 2H); 3.62-3.68 (m, 1H); 3.38-3.50 (m, 2H); 3.43 (s, 3H, -OMe); 2.35 (m, 1H); 1.88 (m, 1H); 1.67 (bs, 1H, -OH). $^{13}$C-NMR: 138.32, 129.26, 128.70, 128.45, 128.06, 97.44, 74.15, 72.62, 71.35, 71.22, 70.93, 62.65, 55.15, 30.07.

**Methyl 2,4-Di-O-benzyl-3,6-dideoxy-6-iodo-α-D-*ribo*-hexopyranoside (37).-** To a solution of **36** (7.00 g, 19.5 mmol) in toluene (100 mL) were added imidazole (4.00 g, 58.7 mmol), $PPh_3$ (6.15 g, 23.4 mmol) and iodine (5.95 g, 23.4 mmol) with vigorous stirring. After 4 h at room temperature the solvent was removed *in vacuo*, the crude residue purified by flash chromatography with toluene/ethyl acetate (25/1) as eluent, affording **37** as colorless oil (8.05 g, 88 %). $[\alpha]_D^{20}$ = +77.5° (c 4.2). $^1$H-NMR: 7.31-7.41 (m, 10H); 4.72 (d, 1H, J = 3.0); 4.61-4.64 (AB-system, 2H, J = 12.5); 4.49 and 4.66 (AB-system, 2H, J = 11.2); 3.50 (s, 3H, -OMe); 3.44-3.58 (m, 3H); 3.25-3.36 (m, 2H); 2.40 (ddd, 1H, J = 11.5, 4.5, 4.4); 1.93 (ddd, 1H, J = 11.5, 3). $^{13}$C-NMR: 138.25, 138.00, 128.66, 128.02, 97.52, 76.10, 74.14, 71.39, 70.91, 70.08, 55.38, 29.86, 8.12.

**(2*R*, 4*S*)-Dibenzyloxyhex-5-enal (38).-** A solution of iodide **37** (4.80 g, 10.24 mmol) in THF (5 mL) was injected into a freshly prepared suspension of Zn/Ag-graphite (30 mmol)[6] in THF (50 mL) at room temperature. After stirring for 10 min, the graphite was filtered off, washed with THF (80 mL) in several portions, the combined filtrates were evaporated and the residue purified by flash chromatography (toluene/ethyl acetate = 25/1) affording enal **38** as colorless oil (2.74 g, 86%). $[\alpha]_D^{20}$ = +8.2° (c 3.1). $^1$H-NMR: 9.70 (d, 1H, J = 1.1); 7.27-7.39 (m, 10H); 5.78 (ddd, 1H, J = 16.4, 9, 8); 5.25 (d, 1H, J = 16.4); 5.26 (d, 1H, J = 9); 4.58 and 4.73 (AB-system, 2H, J = 12); 4.40 and 4.58 (AB-system, 2H, J = 11.5); 4.11 (dt, 1H, J = 10.5, 4.8); 3.94 (vt, 1H, J = 5.1); 2.16 (ddd, 1H); 1.95 (dd, 1H). $^{13}$C-NMR: 202.40, 138.36, 137.97, 137.66, 129.13, 128.58, 128.39, 128.03, 127.93, 127.58, 118.01, 80.66, 76.36, 72.35, 70.50, 37.18.

**(2*R*, 4*S*)-Dibenzyloxy-1,1-dimethoxy-hex-5-ene (39).-** A solution of **38** (1.03 g, 3.32 mmol) and p-toluenesulfonic acid monohydrate (~0.1 g) in MeOH (10 mL) and trimethyl orthoformate (10 mL) is stirred for 15 min at room temperature. Sat. $NaHCO_3$ (10 mL) is added, the mixture extracted with $CH_2Cl_2$ (30 mL) in three portions, the organic layer dried ($Na_2SO_4$), the solvent evaporated *in vacuo* and the crude acetal purified by column chromatography with toluene/ethyl acetate (25/1) as eluent. Colorless oil (1.15 g, 97%). $[\alpha]_D^{20}$ = -2.1° (c 5.6); $^1$H-NMR: 7.29-7.39 (m, 10H); 5.78 (ddd, 1H, J = 17.2, 10.2, 8); 5.29 (d, 1H, J = 10.2); 5.14 (d, 1H, J = 17.2); 4.58 and 4.77 (AB-system, 2H, J = 12); 4.43 and 4.62 (AB-system, 2H, J = 12); 4.33 (d, 1H, J = 5.8, 1.0); 4.04 (vq, 1H, J = 5.8); 3.57 (ddd, 1H, J = 8.4, 4.0); 3.45 and 3.47 (s, 3H each, -OMe); 2.03 (m, 1H); 1.94 (m, 1H); $^{13}$C-NMR: 138.93, 129.19, 128.45, 128.02, 127.93, 127.62, 127.51, 118.09, 107.45, 77.98, 76.51, 72.78, 70.19, 55.77, 55.46, 36.70.

**(2*R*, 4*R*)-Dibenzyloxy-6-tert-butyldiphenylsilyloxy-1,1-dimethoxyhexane (41).-** To a solution of **39** (0.81 g, 2.27 mmol) in THF (10 mL) was added 9-BBN dimer (1.47 g, 6.00 mmol) and the mixture was stirred for 3 h at room temperature under Ar. After cooling to 0°C NaOH (3N, 1.8 mL) followed by $H_2O_2$ (30%, 1.8 mL) were slowly added, the mixture reacted for 30 min, quenched with brine and extracted with diethyl ether (50 mL) in several portions. The combined organic layers were dried, evaporated and the crude alcohol silylated without further purification. For analytical purposes, however, a 50 mg sample of the crude product was chromatographed (toluene/ethyl acetate = 25/1). The alcohol thus obtained showed the following analytical and spectral properties: $[\alpha]_D^{20}$ = +28.8° (c 3.4); $^1$H-NMR: 7.26-7.44 (m, 10H); 4.57 and 4.77(AB-system, 2H, J = 11.5); 4.47 and 4.61 (AB-system, 2H, J = 11.5); 4.31 (d, 1H, J = 5.1); 3.77 (m, 1H); 3.67 (m, 2H); 3.53 (m, 1H); 3.46, 3.49 (s, 3H each, -OMe); 2.60 (bs, 1H, -OH); 1.85 and 2.00 (ddAB-system, 2H, J(AB) = 13); 1.68 and 1.71 (vq, 2H, J = 5.8). $^{13}$C-NMR: 138.68, 135.73, 135.04, 128.63, 128.58, 128.35, 128.16, 127.88, 107.52, 76.51, 75.85, 73.00, 70.83, 60.84, 56.15, 55.82, 36.37, 34.39.

For silylation the crude product was dissoved in DMF (8 mL), imidazole (0.30 g, 4.40 mmol) and t-Bu$Ph_2SiCl$ (0.80 mL, 3.10 mmol) were added and the mixture stirred for 12 h at room temperature. Addition of HCl (0.1N, 5 mL), extraction with $CH_2Cl_2$ (30 mL) in three portions, drying of the organic phases over $Na_2SO_4$, evaporation of the solvent and flash chromatography (toluene/ethyl acetate = 25/1) of the remaining syrup afforded the anticipated compound as colorless oil (1.20 g, 86%). $[\alpha]_D^{20}$ = +8.6° (c 7.7); $^1$H-NMR: 7.27-7.83 (m, 20H); 4.65 and 4.83 (AB-system, 2H, J = 11.5); 4.51 and 4.63 (AB-system, 2H, J = 11.5); 4.37 (d, 1H, J = 5.2); 3.87-3.97 (m, 3H); 3.66 (m, 1H); 3.49, 3.54 (s, 3H each, -OMe); 1.89-2.01 (m, 4H); 1.15 (s, 9H). $^{13}$C-NMR: 139.22, 138.96, 135.79, 135.63, 135.05, 134.26, 129.76, 128.47, 128.06, 128.00, 127.88, 127.84, 127.67, 127.51, 107.49, 77.01, 73.49, 73.00, 70.98, 60.93, 55.89, 55.69, 37.86, 35.31, 27.16, 26.84, 19.43.

**(2*R*, 4*R*)-Dibenzyloxy-6-*tert*-butyldiphenylsilyloxy-hexanal (42).-** To a solution of **41** (1.00 g, 1.63 mmol) in acetone (15 mL) was added p-toluenesulfonic acid monohydrate (~70 mg). After stirring for 6 h, the solution was neutralized with $NEt_3$, the solvent removed *in vacuo* and the residue subjected to column chromatography with toluene/ethyl acetate (25/1) as eluent. Colorless oil (879 mg, 95%). $[\alpha]_D^{20}$ = +16.3° (c 2.1); $^1$H-NMR: 9.70 (d, 1H, J = 1.3); 7.07-7.94 (m, 20H); 4.65 and 4.78 (AB-system, 2H, J = 11.8); 4.58 (s, 2H); 4.08 (vt, 1H, J = 5.9); 4.00 (vt, 1H, J = 5.1); 3.90 (vq, 2H, J = 10); 2.16 (m, 1H); 1.84 - 2.02 (m, 3H); 1.26 (s, 9H); $^{13}$C-NMR: 202.88, 138.59, 137.73, 136.05, 135.57, 135.39, 135.27, 135.05, 134.69, 134.50, 133.99, 129.86, 129.78, 129.61, 129.48, 129.22, 129.15, 128.67, 128.48, 128.08, 127.90, 127.68, 80.90, 72.47, 71.48, 71.35, 60.66, 37.19, 36.28, 27.16, 19.40.

**Methyl (2*R*, 4*R*)-Dibenzyoxy-6-*tert*-butyldiphenylsilyloxy-hexanoate (44).-** Compound **42** (1.10 g, 1.94 mmol) was dissolved in DMF (50 mL) containing MeOH (1 mL, 19.7 mmol). After stirring for 30 min PDC (7.70 g, 11.40 mmol) was added and the mixture kept for 48 h at room temperature. Addition of

water (20 mL) followed by extraction with cyclohexane (60 mL) in three portions, evaporation of the solvent and chromatographic purification of the residue with petrol ether/ethyl acetate (40/1) as eluent afforded the pure product as colorless oil (0.79 g, 68%). $[\alpha]_D^{20}$ = -0.8° (c 2.0); $^1$H-NMR: 7.27-7.77 (m, 20H); 4.47 and 4.73 (AB-system, 2H, J = 11.6); 4.45 and 4.50 (AB-system, 2H, J = 11.1), 4.13 (vt, 1H, J = 5.9); 3.93 (quint., 1H, J = 5.9); 3.77-3.81 (m, 2H); 3.66 (s, 3H, -OMe); 2.03-2.21 (m, 2H); 1.80-1.88 (m, 2H); 1.10 (s, 9H). $^{13}$C-NMR: 173.31, 138.94, 137.83, 135.82, 135.08, 134.14, 129.84, 128.61, 128.45, 128.22, 128.15, 128.03, 127.96, 127.90, 127.62, 75.45, 72.90, 72.55, 71.45, 60.68, 51.94, 37.95, 37.43, 27.16, 26.84, 19.43.

**Dimethyl [(3*R*, 5*R*)-Dibenzyloxy-7-*tert*-butyldiphenylsilyloxy-heptan-2-on-1-yl] Phosphonate (45).**- n-BuLi (1.6M in hexane, 780 µl, 1.30 mmol) was added to a solution of dimethyl methylphosphonate (140 mg, 1.30 mmol) in THF (12 mL) at -78°C under Ar. After 30 min a solution of **44** (300mg, 0.50 mmol) in THF (1 mL) was injected and the mixture stirred for 3 h at that temperature. For work-up sat. $NH_4Cl$ (5 mL) was added at 0°C followed by extraction with $CH_2Cl_2$ (30 mL) in several portions. After drying with $Na_2SO_4$ the combined organic layers were evaporated and the crude ketophosphonate purified by flash chromatography with toluene/ethyl acetate (25/1) as eluent. Yield: 312 mg (90%) as colorless oil; $[\alpha]_D^{20}$ = -16.1° (c 1.3); $^1$H-NMR: 7.23-7.68 (m, 20H); 4.48 and 4.68 (AB-system, 2H, J = 11.7); 4.35 and 4.41 (AB-system, 2H, J = 11.1); 4.15 (vt, 1H, J = 5.1); 3.88 (m, 1H); 3.78 (m, 2H); 3.73 (d, 3H, J(P, POMe) = 2.8); 3.70 (d, 3H, J(P, POMe') = 2.1); 3.10 (d, 2H, J(P, H-2) = 21.8); 2.03 and 2.09 (ddAB-system, 2H, J(AB) = 13); 1.82 (dt, 2H, J(AB) = 12.8). $^{13}$C-NMR: 202.72, 138.66, 137.92, 135.82, 134.05, 129.89, 128.67, 128.53, 128.19, 128.09, 127.93, 127.74, 81.58, 72.87, 72.49, 71.38, 60.64, 53.07, 37.65, 37.20, 36.79 [J(P, C-1) = 129], 27.16, 19.43.

**Transposition Sequence: Compound 48 (Mixture of Diastereoisomers).**- Trimethylsilylmethylmagnesium chloride (1M in diethyl ether, 9 mL, 9 mmol) was added under Ar to a solution of **38** (660 mg, 2.13 mmol) in THF (30 mL). After stirring for 12 h at ambient temperature the reaction was quenched with sat. $NH_4Cl$ (10 mL) and the aqueous phase extracted with ethyl acetate (20 mL in two portions). Drying the combined organic layers ($Na_2SO_4$) and evaporation of the solvent afforded compound **46** as mixture of stereoisomers which was used without further purification. $OsO_4$ (~5 mg) and N-methylmorpholine--N-oxide (1.00g, 7.4 mmol) were added to a solution of the crude **46** in acetone (5 mL). After stirring for 48 h at room temperature, the solvent was evaporated and the residue purified by flash chromatography with $CHCl_3$/MeOH (9/1) as eluent. The product (**47a**, 837 mg, 91%) (mixture of stereoisomers) was dissolved in $CH_2Cl_2$ (5 mL), 2,2-dimethoxypropane (0.71 mL, 5.8 mmol) and p-toluenesulfonic acid (50 mg) were added. Stirring for 20 min at ambient temperature, neutralization of the mixture with $NEt_3$ and evaporation of the solvent followed by a flash chromatography using toluene/ethyl acetate (25/1) as eluent afforded a mixture of the diastereoisomers of dioxolane **47b** (796 mg, 87%) which were eliminated to **48** without further characterization. This was achieved by addition of $BF_3.Et_2O$ (50 µL) to a solution of **47b** in $CH_2Cl_2$ (5 mL), stirring the reaction mixture for 2 h under Ar, neutralization with $NEt_3$, evaporation of the solvent *in vacuo* and chromatographic purification (toluene/ethyl acetate 7/1) of the residue. Thus compound **48** was obtained as colorless oil (425 mg, 66%). $^1$H-NMR (diagnostic values for the major isomer): 5.70 (ddd, 1H); 5.30 (d, 1H); 5.21 (d, 1H); 4.60 and 4.71 (AB-system, 2H); 4.36 and 4.54 (AB-system, 2H); 1.90-2.05 (m, 1H); 1.65-1.78 (m, 1H); 1.46, 1.37 (s, 3H each). $^{13}$C-NMR (major isomer): 138.86, 118.33, 109.33, 78.85, 76.03, 72.74, 70.35, 66.18, 63.26, 38.13, 26.83, 25.55; (resolved signals of the minor isomer): 26.71, 24.84.

**Compound 49 (Mixture of Diastereoisomers).**- A solution of **48** (350 mg, 0.92 mmol) and 9-BBN dimer (560 mg, 2.3 mmol) in THF (10 mL) was stirred under Ar at ambient temperature for 2 h, followed by slow addition of NaOH (3M, 1.2 mL) and $H_2O_2$ (30%, 1.2 mL). After another 30 min at that temperature, the mixture was washed with brine (10 mL), the aqueous layer extracted with diethyl ether (30 mL in several portions), the combined organic layers dried ($Na_2SO_4$), the solvent removed *in vacuo* and the residue purified by chromatography (toluene/ethyl acetate 7/1) affording **49** as colorless oil (341 mg, 93%). $^1$H-NMR (major isomer, [resolved signals of the minor isomer], ratio major/minor ≈ 2.7/1): 7.26-7.38 (m, 10H); 4.71 [4.77] 4, 60, 4.58 [4.57] (m, 4H); 4.16 [4.26] (dd, 1H, J = 6.5, 12); 4.07 [3.99] (dd, 1H, J = 6.5); 3.89 (dd, 1H, J = 6.5, 8); 3.50-3.84 (m, 4H); 1.90-2.05 (m, 1H); 1.65-1.80 (m, 3H); 1.45 [1.47], 1.38 (s, 3H each). $^{13}$C-NMR (major isomer [resolved signals of the minor isomer]): 109.46 [109.72], 78.63 [78.27], 76.25 [76.56], 75.55, 72.90 [72.77], 71.03, 66.41 [66.08], 60.68, 36.41 [36.22], 35.96, 26.74, 25.49.

**Compound 50 (Mixture of Diastereoisomers).**- Addition of benzoyl chloride (200 µL, 1.70 mmol) and p-dimethylaminopyridine (≈70 mg) to a solution of **49** (340 mg, 0.85 mmol) in $CH_2Cl_2$ (5 mL) and pyridine (200 µl), stirring for 12 h at ambient temperature, extractive work-up with HCl (0.1N, 5 mL) and $NaHCO_3$ sat. (5 mL), drying of the organic layer ($Na_2SO_4$), evaporation of the solvent and final flash chromatography (toluene/ethyl acetate 25/1) afforded **50a** as colorless oil (381 mg, 89%). $^1$H-NMR (major isomer [signals of the minor isomer where resolved), ratio major/minor isomer ≈ 3/1): 7.22-8.00 (m, 15H); 4.49-4.77 (m, 4H); 4.40-4.47 (m, 2H); 4.18 [4.29] and 4.07 [4.00] (dd, 1H each); 3.82-3.93 (m, 2H); 3.72 [3.61] (m, 1H); 1.93-2.10 (m, 3H); 1.77-1.84 (m, 1H); 1.45 [1.47], 1.37 (s, 3H each). $^{13}$C-NMR (major isomer [minor isomer, when resolved]): 166.71, 109.43, 78.69, [78.21], 76.54, [73.33], 73.07, 72.91, 72.81,

[71.28], 71.19, 66.56, [66.24], 66.08, 62.03, 36.54, [35.18], 33.72, [33.60], 26.76, 25.48. **50a** (300 mg, 0.60 mmol), dissolved in THF (5 mL) and p-TsOH.$H_2O$ (70 mg) were stirred for 12 h, the mixture neutralized with $NEt_3$ and the solvent removed *in vacuo* affording **50b**, which was used without further purification in the next step. For analytical purposes, however, a ≈50 mg sample was purified by flash chromatography with toluene/ethyl acetate (1/1) as eluent. $^1$H-NMR (major isomer, [resolved signals of the minor component], ratio major/minor isomer ≈ 3:1): 7.22-8.00 (m, 15H); 4.43-4.64 (m, 6H); 3.63-3.96 (m, 5H); 3.37 (bd, 1H, -OH); 2.58 [2.86] (bs, 1H, -OH); 1.86-2.14 (m, 4H). $^{13}$C-NMR (diagnostic values, major isomer [resolved signals of the minor isomer]): 166.74, 77.71, 76.87, 73.02, [72.92], 72.31, [72.25], 71.43, [71.27], [64.21], 63.89, [61.82], 61.76, [34.98], 34.80, [33.50], 33.26.

**6-Benzoyloxy-(2*S*,4*S*)-dibenzyloxyhexanal (51).-** To a solution of the crude **50b** as obtained in the previous step in a biphasic mixture of $CH_2Cl_2$ (15 mL) and water (15 mL) was added $NaIO_4$ (300 mg, 1.4 mmol) with vigorous stirring. Stirring was continued for 12 h, the layers were separated, the aqueous phase extracted twice with $CH_2Cl_2$ (20 ml each), the combined organic phases dried ($Na_2SO_4$), the solvent evaporated and the residue purified on a short column with toluene/ethyl acetate as eluent thus affording the title compound as colorless oil (201 mg, 78%). $[\alpha]_D^{20}$ = -19.7° (c 3.8). $^1$H-NMR: 9.67 (s, 1H); 7.26-8.03 (m, 15H); 4.57 and 4.74 (AB-system, 2H, J = 12); 4.53 (d, 2H, J = 4); 4.43 (dt, 2H, J = 2, 8); 3.90-4.00 (m, 2H); 2.02-2.09 (m, 4H). $^{13}$C-NMR: 202.56, 166.65, 138.25, 137.57, 133.11, 129.77, 129.26, 128.74, 128.58, 128.25, 128.19, 128.13, 127.90, 127.77, 80.73, 72.65, 72.22, 71.52, 61.69, 35.80, 33.34.

**Enone (54).-** Ketophosphonate **45** (82 mg, 0.12 mmol) in DME (2 mL) was deprotonated under Ar with NaH (80% suspension in mineral oil, 4 mg, 0.12 mmol) at 0°C, followed by stirring at 40°C for 20 min. After the solution had been cooled to -65°C, a solution of aldehyde **51** (52 mg, 0.12 mmol) in DME (1 mL) was added, the mixture allowed to warm to room temperature over a period of 2 h and stirring continued at that temperature for another 2 h. After addition of sat. $NaHCO_3$ (4 mL), extractive work-up with $CH_2Cl_2$ (20 mL in several portions), drying of the organic phase ($Na_2SO_4$), evaporation of the solvent and flash chromatography with toluene/ethyl acetate (7/1) as eluent, enone **54** was obtained as *(E)*-isomer only. Colorless oil (99 mg, 86%). $[\alpha]_D^{20}$ = -3.8° (c 2.7). $^1$H-NMR: 7.15-7.99 (m, 35H); 6.92 (dd, 1H, J = 5.9); 6.65 (d, 1H, J = 15.7); 4.55 (m, 1H); 4.38-4.51 (m, 9H); 4.26 (d, 1H, J = 11.5); 4.07-4.13 (m, 2H); 3.87-3.92 (m, 1H); 3.73-3.82 (m, 2H); 1.68-2.12 (m, 8H); 1.06 (s, 9H). $^{13}$C-NMR: 200.23, 166.70, 147.21, 138.90, 138.53, 138.11, 138.06, 137.80, 135.82, 134.15, 133.10, 130.64, 129.82, 129.29, 128.65, 128.48, 128.03, 127.93, 127.64, 125.57, 125.24, 81.58, 75.75, 73.10, 72.87, 72.42, 71.55, 71.35, 71.16, 61.90, 60.74, 39.63, 37.54, 37.44, 33.50, 27.19, 19.46.

**(3*R*,5*S*)-Dibenzyloxy-1-methoxyhepta-1,6-diene (52).-** To a suspension of thoroughly dried methoxymethyltriphenylphosphonium chloride (690 mg, 2.00 mmol) in diethylether (8 mL) under Ar was added n-BuLi (1.6M in hexane, 1.21 mL, 1.93 mmol) at -5°C. After stirring the orange-red suspension for 30 min at ambient temperature a solution of **38** (300 mg, 0.97 mmol) in diethyl ether (10 mL) was slowly added at -70°C. After the mixture was allowed to warm to room temperature, addition of water (10 mL) and standard work-up flash chromatography of the crude product using toluene/ethyl acetate (25/1) as eluent afforded the title compound as syrup (230 mg, 70%). $[\alpha]_D^{20}$ = + 2.5° (c 0.8); $^1$H-NMR: 7.34-7.44 (m, 10H); 6.45 (d, 1H, J = 12.7, (E)-isomer); 6.21 (d, 1H, J = 6.3, (Z)-isomer) [(E):(Z) = 1.8:1]; 5.87 (m, 1H); 5.30 (m, 2H); 4.71 (m, 3H); 4.45 (m, 2H); 4.00 (m, 2H); 3.66 (s, 3H, (Z)-isomer); 3.60 (s, 3H, (E)-isomer); 2.30 (m, 1H); 1.77 (m, 1H). $^{13}$C-NMR: 150.89 (E), 149.25(Z); 138.99 (E), 139.06 (Z); 139.19, 129.22, 128.45, 128.08, 128.03, 127.93, 127.57, 127.47, 127.39; 117.35(E), 117.19(Z); 107.65(Z), 103.31(E); 77.82(E), 78.44(Z), 74.55, 70.61, 70.28, 70.19, 69.54, 69.40; 59.90(Z), 56.15(E); 42.88(E), 42.01(Z).

**5-O-Benzyl-2(*Z*),6-heptadien-1,5(*S*)-diol (53).-** To a solution of **52** (100 mg, 0.3 mmol) and $NaBH_3CN$ (100 mg, 1.4 mmol) in diethyl ether (5 mL) was added HCl (6N) at such a rate, that the pH of the solution was kept between 5 and 6. After TLC showed complete conversion of the substrate (10 min), the mixture was diluted with water (10 ml) extracted with ether (30 mL in several portions), the organic layers were dried over $Na_2SO_4$, the solvent evaporated and the residue purified by column chromatography with toluene/ethyl acetate (15/1) as eluent. Thus, the product was obtained as colorless oil (42 mg, 65%). $[\alpha]_D^{20}$ = +29.4° (c 2.7); $^1$H-NMR: 7.28-7.40 (m, 5H); 5.78 (ddd, 1H); 5.69-5.73 (m, 2H); 5.28 (d, 1H, J = 9.1); 5.26 (d, 1H, J = 15); 4.39 and 4.62 (AB-system, 2H, -$CH_2$Ph, J = 12); 4.08 (d, 2H, J = 3.3); 3.36 (d, 1H, J = 3.1); 2.37 (m, 2H); 1.91 (bs, 1H, -OH). $^{13}$C-NMR: 138.86, 128.70, 128.51; 138.60; 131.87, 128.38; 117.55; 80.24; 70.34; 63.71; 38.58.

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