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# STEREOCONTROLLED SYNTHESIS OF ERYTHRONOLIDES A AND B IN A (C5-C9) + (C3-C4) + (C1-C2) + (C11-C13) SEQUENCE FROM 1,6-ANHYDRO-β-D-GLYCOPYRANOSE (LEVOGLUCOSAN). PART 1. SYNTHESIS OF C1-C10 AND C11-C13 SEGMENTS

A.F.SVIRIDOV, V.S.BORODKIN, M.S.ERMOLENKO, D.V.YASHUNSKY, N.K.KOCHETKOV*

N.D.Zelinsky Institute of Organic Chemistry, Academy of Sciences of the U.S.S.R., Moscow, U.S.S.R.

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Abstract. An approach to the synthesis of aglycones of macrolide antibiotics erythromycine A and B is discussed and preparation of common C1-C10 and C11-C13 segments starting from levoglucosane is described.

Erythronolides A and B (1A and 1B, Scheme 1) represent perfect synthetic targets suitable for solution of many general problems of stereocontrolled synthesis of macrolide antibiotics and other natural polyketides. And that is why several total syntheses of erythromycin[1], and erythronolides A[2] and B[3] have been published during the last decade.

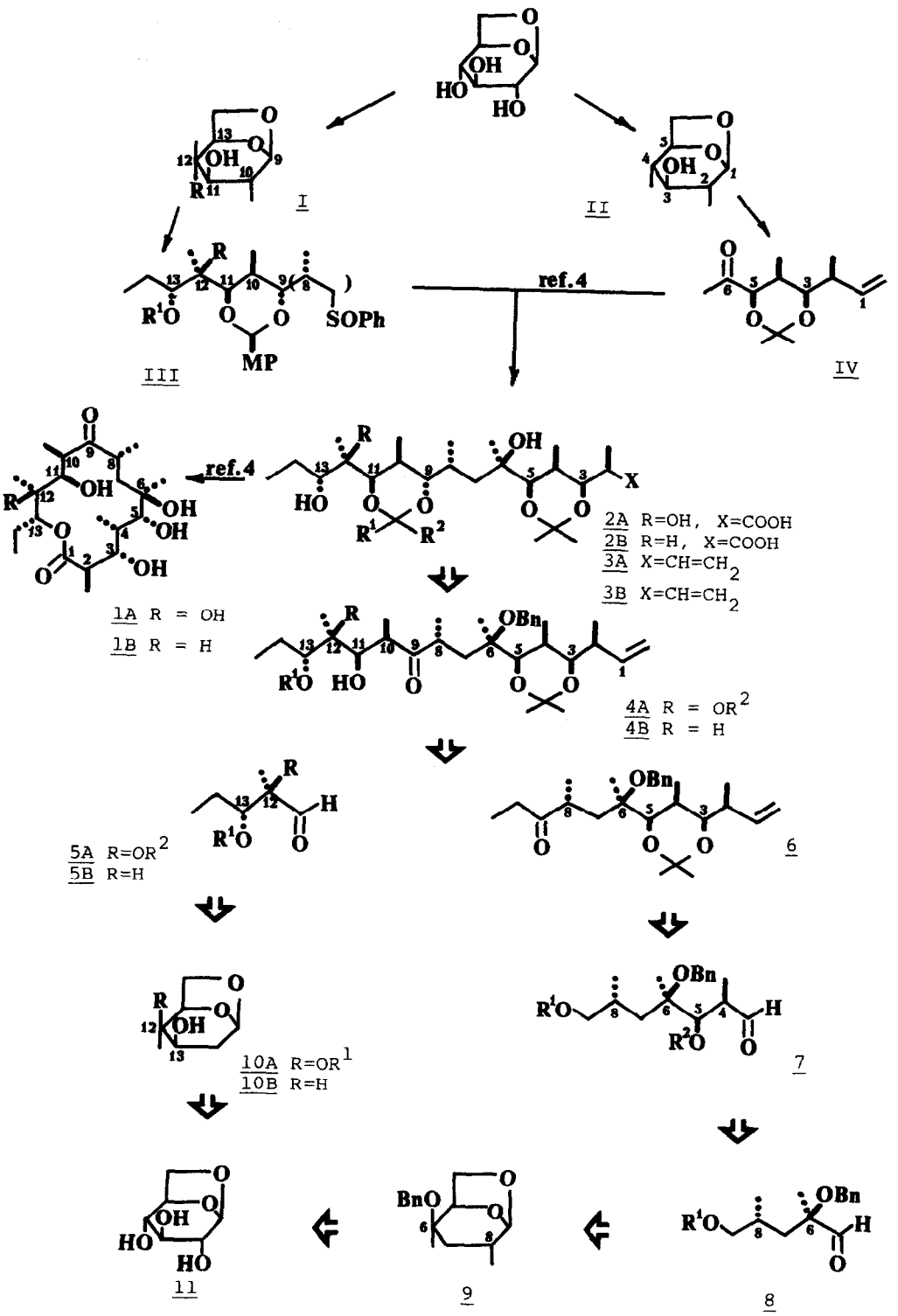
In our previous publication[4] was described a stereocontrolled synthesis of erythronolides A and B from the single carbohydrate precursor, levoglucosane. The connection of carbohydrate-derived C7-C13 (III) and C1-C6 (IV) segments (Scheme 1, top) resulted in compounds 3A and 3B which served as the key intermediates of the synthesis. Noteworthy that the majority (9 of 11) of chiral centres in 3A and 3B originated from the "modified carbohydrates" (I and II).

Here we report the synthesis of erythronolides A and B according to a new strategy which is based on the use of acyclic carbohydrate-derived segments as the chiral substrates for the sequence of unified reactions aimed at the stereoselective construction of contiguous chiral centres of the type "hydroxyl-methyl-hydroxyl". This strategy combines advantages of "carbohydrate" and "acyclic" approaches to the synthesis of compounds of polyketide origin and can be of interest for the synthesis of related structures.

## 1. Retrosynthetic Analysis of Erythronolides A and B

Structural similarity of the derivatives 3A and 3B makes possible their synthesis through aldol addition of the ketone 6 enolate (6 being the common

Scheme 1


I
II
III
IV
ref.4
ref.4
1A R = OH
1B R = H
2A R=OH, X=COOH
2B R=H, X=COOH
3A X=CH=CH2
3B X=CH=CH2
4A R = OR2
4B R = H
5A R=OR2
5B R=H
6
7
8
9
10A R=OR1
10B R=H
11

C1–C10 segment of carbon chains of the both target structures) to the aldehydes 5A and 5B followed by selective reduction of the hydroxyketones 4A and 4B which would ensure the creation of a required configuration of the C9-centre. Retrosynthetic transformation of the structures 5A and 5B yields, in turn, bicyclic derivatives 10A and 10B. Approaches to their synthesis from levoglucosan 11 as a common carbohydrate precursor have already been elaborated by us[5,6].

Contiguous chiral centres C2–C5 in the ketone 6 could supposedly be established by a repeated $S_E'$-reaction of an crotyl-metallic reagent with aldehydes 7 and 8 The latter could be prepared from the bicyclic derivative 9 (Scheme 1) which, in turn, also originates from levoglucosan 11.

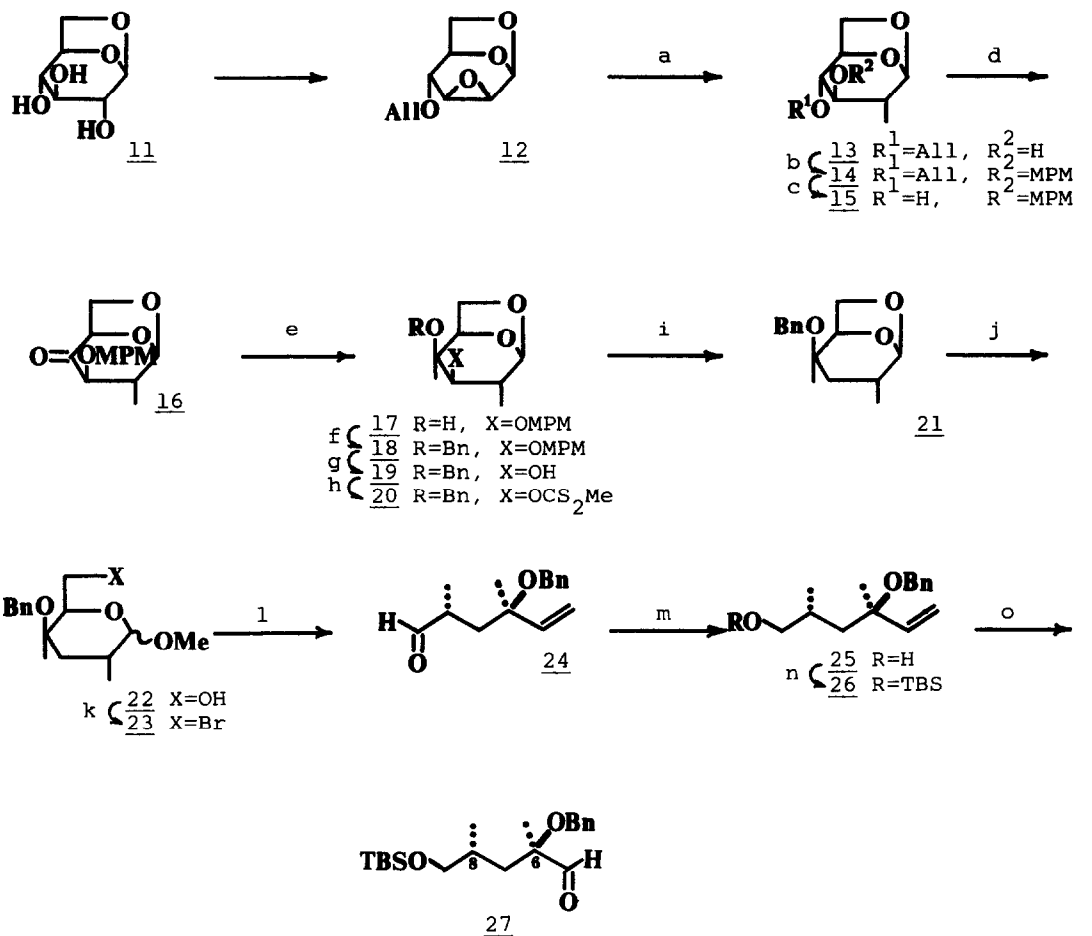
## 2. Synthesis of the C1–C10 Segment of Erythronolides A and B

The initial step for an access to the title segment was the synthesis of compound 21 (Scheme 2) which is a bicyclic precursor for the C5–C9 segment of erythronolides A and B. This was performed in a sequence similar to that described[7] for the synthesis of a di-O-benzyl analogue of compound 18 followed by deoxygenation from C3. This necessitated differential protection of secondary and tertiary hydroxyls. To this end the secondary alcohol 13, obtained by ring-opening of the oxirane 12[8] with $Me_2Mg$ in ether, was converted into the *p*-methoxybenzyl (MPM) ether 14 and then, conventionally, into the tertiary alcohol 17. Benzyl protection for the hydroxyl group in 17 (17 -> 18) was chosen to meet requirements of subsequent stereocontrolled addition of tri-*n*-butylcrotyl tin. Selective removal of the MPM-protecting group from 18[9] afforded the monohydroxyl derivative 19 which was subjected to Barton deoxygenation[10] to yield 21.

Opening of 1,6-anhydro-ring in 21 by methanolysis gave a mixture (9:2) of α- and β-methyl glycosides 22 which were converted without separation into respective 6-bromo-derivatives 23. Treatment of the latter mixture with activated Zn dust in boiling aqueous *i*-PrOH (cf. [11]) resulted in a aldehyde 24 which was then converted into the target C5–C9 segment of erythronolides A and B, aldehyde 27, in 35% overall yield (from the oxirane 12).

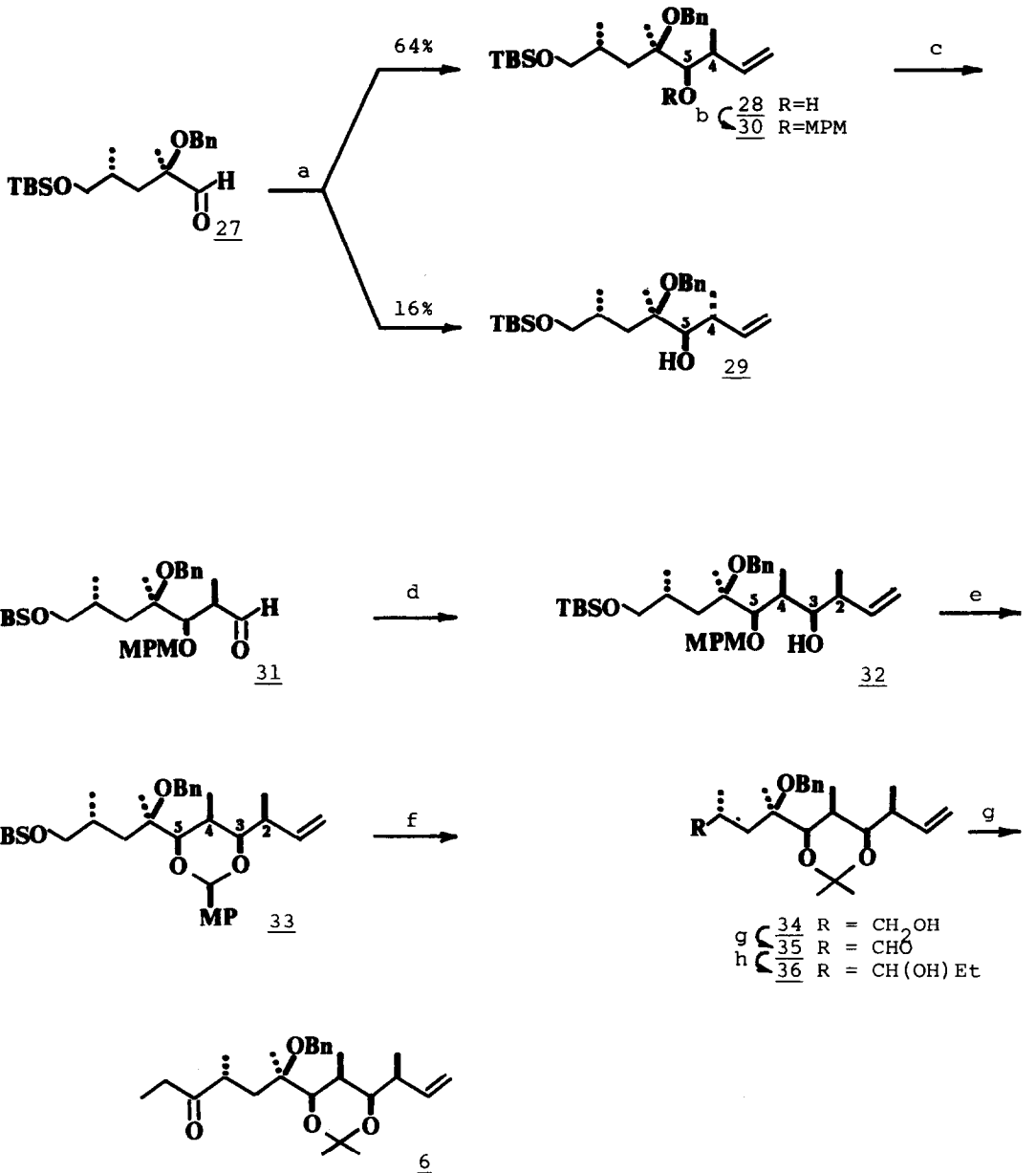
Stereocontrolled addition of tri-*n*-butylcrotyl tin to aldehydes 8 and then to 7 (Scheme 1) derived therefrom was supposed to be the route to the ketone 6. This reagent is known to exhibit high *syn*-selectivity of Lewis acid promoted addition to aldehydes[12,13] irrespective of double-bond geometry that makes it very attractive from preparative point of view. Recent studies revealed that diastereoselectivity of addition of tri-*n*-butylcrotyl tin to chiral α- and β-alkoxyaldehydes can be controlled by optimisation of reaction conditions and structure of a substrate[13,14].

Scheme 2




a: $Me_2Mg/Et_2O$, 100%; b: NaH, MPMCl/DMF, 95%; c: t-BuOK/DMSO; $Hg(OAc)_2/Me_2CO$, 99%; d: DMSO, $(COCl)_2$, $Et_3N/CH_2Cl_2$, $-60^{\circ}$, 97%; e: MeMgBr/THF, $-50^{\circ}$, 98%; f: NaH, BnBr/DMF, 93%; g: DDQ/$CH_2Cl_2$-$H_2O$, 85%. h: NaH, $CS_2$, MeI/THF; i: $Bu_3SnH$, AIBN/$PhCH_3$,Δ, (h,i 86%); j:5% HCl-MeOH 100%; k: $CBr_4$, $PPh_3$/Py, $+60^{\circ}$, 96%; l: Zn/i-PrOH-$H_2O$ (14:1), 96%; m: $LiAlH_4/Et_2O$, $-50^{\circ}$; n: TBSCl, ImD/DMF, (m,n 80%); o: $O_3/CH_2Cl_2$-1% Py, $-78^{\circ}$, 85%.

Scheme 3




a: Tri-n-butylcrotyl tin, $MgBr_2/CH_2Cl_2$, +25°, 50 hrs; b: NaH, MPMCl/DMF, 73%; c: NMO, $OsO_4/Me_2CO$-$H_2O$; $NaIO_4$/THF-$H_2O$, 92%; d: tri-n-butylcrotyl tin $BF_3.Et_2O/CH_2Cl_2$, -78°, 70%; e: DDQ, MS 3A/$CH_2Cl_2$, 81%; f: $Me_2CO$, DMP, TsOH $H_2O$, 90%; g: $(COCl)_2$, DMSO, $Et_3N/CH_2Cl_2$, -60°; h: EtMgBr/THF, -50°, (g,h,g 78%).

The conditions for addition of this reagent to the aldehyde 8 (Scheme 3) were chosen to ensure chelate control of the process and this necessitated the use of benzyl protection of the α-hydroxyl and $MgBr_2$ as the promoter[13]. Under conditions found the homoallylic alcohols 28 and 29 were produced in a ratio of 4:1 and total yield of 80%. The chelate-controlled, $MgBr_2$-promoted addition of tri-*n*-butylcrotyl tin to the aldehyde 8 proceeds with exceptional diastereofacial selectivity and moderate "simple" selectivity (for structural elucidation of 28 and 29 see the last paragraph in this paper). Further steps in the synthesis of the C1-C10 segment from the homoallylic alcohol 28 involved protection of the secondary hydroxyl and conversion of the methylene group into aldehyde. Ozonolysis of compound 30 proceeded with satisfactory yield (75%) for dilute solutions ($10^{-3}$ M) only. At the same time, the use of a two-step "hydroxylation-periodate oxidation" sequence allowed to prepare the required aldehyde 31 in 92% yield.

Creation of a proper stereochemistry of the C2 and C3 centres required a reaction of tri-*n*-butylcrotyl tin to the aldehyde 31 to be promoted with the monodentate Lewis acid, $BF_3.Et_2O$, which excludes formation of chelated intermediates. Of no lesser importance in effecting high selectivity of the process was the choice of a type of protecting group for the secondary hydroxyl in the β-alkoxyaldehyde 31. Thus aldol addition of tri-*n*-butylcrotyl tin to MPM-ether 31 afforded the required 2;3;4;5-*syn* product 32 in 70% yield while its TBS-analogue reacted to give mainly the product with "unnatural" configuration at C3. These data are in contrast with those reported[14] as one would expect quite an opposite dependence of diastereoselectivity on the nature of protective group.

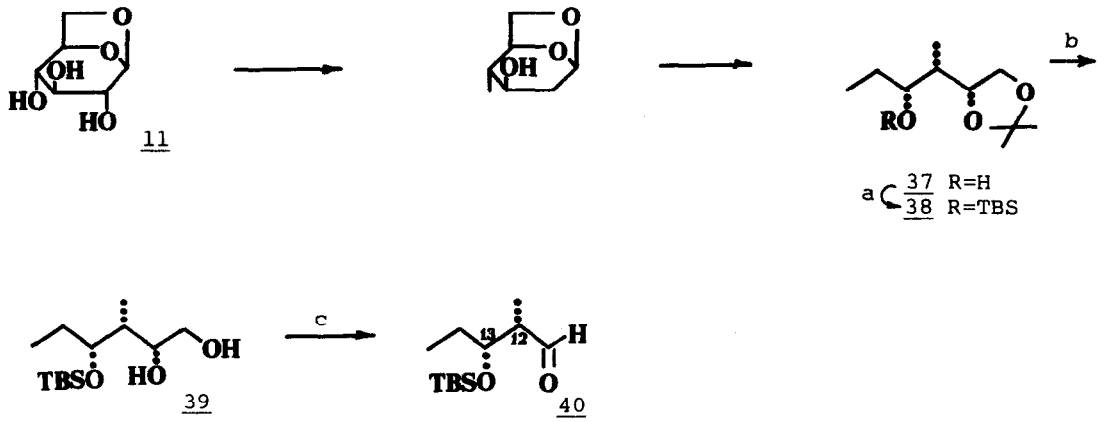
Treatment of 32 with DDQ[15] resulted in formation of a cyclic MP-acetal 33. $^1$H-NMR data point to 3,4,5-*syn* orientation which corresponds to their "natural" configuration in erythronolides. These data are coupling constants ($J_{3,4}=J_{4,5}=1.5$ Hz) and n.O.e at H-3 and H-5 upon pre-irradiation of $H_{acetal}$. The latter fact demonstrates also equatorial position of the aryl group in the MP-acetal 33.

Conversion of 33 into the target ketone 6 was effected through intermediacy of the primary alcohol 34 which was prepared by treating 33 with 2,2-dimethoxypropane-acetone in the presence of equimolar amount of toluene-*p*-sulfonic acid. Its oxidation into the aldehyde 35 followed by Grignard addition yielded the secondary alcohols whose oxidation completes the synthesis of the C1-C10 segment.

3. Synthesis of C11-C13 Segments of Erythronolides A and B

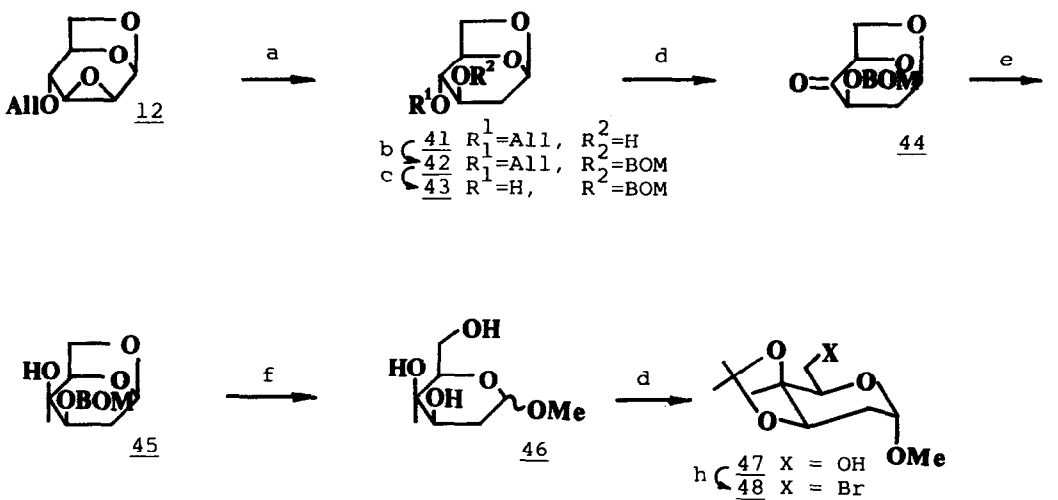
Synthesis of compound 37 (Scheme 4), which is a precursor for the alde-

Scheme 4



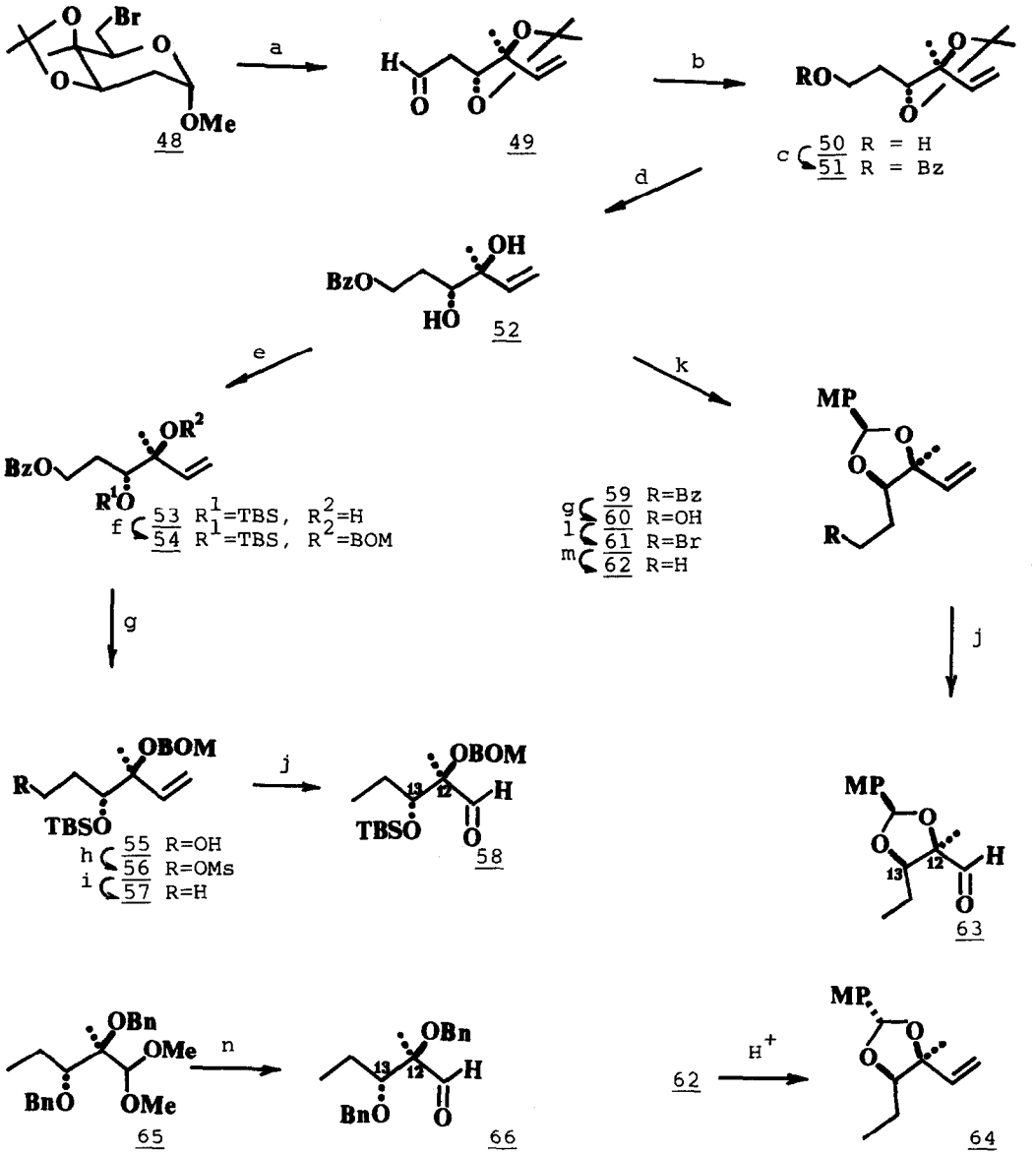
a: TBSOTf, $Et_3N/CH_2Cl_2$, 83%; b: $HS(CH_2)_3SH$, $BF_3.Et_2O/CH_2Cl_2$, -78°, 77%; c: $NaIO_4/THF-H_2O$, 84%.

Scheme 5



a: $LiAlH_4/THF$, Δ, 95%; b: BOMCl, $i\text{-}Pr_2NEt/CH_2Cl_2$, 90%; c: t-BuOK/DMSO, +55°; $Hg(OAc)_2/MeOH-H_2O$, 88%; d: $(COCl)_2$, DMSO, $Et_3N/CH_2Cl_2$, -60°, 92%; e: MeMgBr/THF, 93%; f: 5% HCl-MeOH; g: $Me_2CO$, DMP, CSA, (f,g 68%); h: NBS, $PPh_3$, HMPA, +80°, 77%.

Scheme 6




a: Zn/i-PrOH-$H_2O$; b: $LiAlH_4/Et_2O$, -50°; c: BzCl/Py, (a,b,c 63%); d: $CF_3COOH$, $CH_3CN$, $H_2O$, 83%; e: TBSCl, ImH/DMF, +50°, 80%; f: BOMCl, i-$Pr_2NEt/CH_2Cl_2$, 90%; g: NaOH/MeOH-$H_2O$; h: MsCl, $Et_3N/CH_2Cl_2$; i: $LiBHEt_3$/THF, -78°, (j,h,i 56%); j: $O_3/CH_2Cl_2$-1% Py, -78°, 87%; k: 4-MeOPh$CH_2$OMe, DDQ, MS 3A/$CH_2Cl_2$, 80%; l:$CBr_4$, $PPh_3$/Py; m: $LiBHEt_3$/THF, (g,l,m 73%); n: TsOH $H_2O/CHCl_3$, reflux, 78%.

hyde 40 (C11-C13 segment of erythronolide B), was described by us earlier[5]. Data[16] on high (and necessary) 10,11-*syn*/11,12-*anti* selectivity of addition of Z-(O)-lithium enolate of 6-deoxy analogue of ketone 6 to a 13-O-triethylsilyl analogue of the aldehyde 40 necessitated the use of silyl O-protection. Selective removal of the O-isopropylidene group from 38 (prepared by silylation of 37) could be effected by treatment with propane-1,3-dithiol in the presence of $BF_3 \cdot Et_2O$ at -78°C to give diol 39, periodate cleavage of vicinal glycol in which gave the desired aldehyde 40 in a good yield.

Synthesis of erythronolide A was designed so as to involve addition of the ketone 6 enolate to dialkoxyaldehyde of the type 5A. Three derivatives of this kind were prepared to optimise coupling reaction. Compound 45 (Scheme 5) served as a key intermediate and was prepared following the route similar to that used by us previously in the synthesis of related products[6].

Conversion of 45 into 52, which is a common precursor of aldehydes of the type 5A, followed the lines described for the synthesis of C5-C9 segment (*vide supra*). Methanolysis of 45 gave a mixture of methyl glycosides 46, acetonation of which under conditions of thermodynamic control afforded a bicyclic derivative isolated as α-anomer 47 in 68% yield from 45. Transformation of 47 into 6-bromo derivative 48 was effectively carried out by treatment with NBS-HMPA-$Ph_3P$ at 80°C[17] and reductive elimination gave the aldehyde 49 (Scheme 5). Its subsequent transformations were reduction into alcohol 50 and benzoylation into benzoate 51 in an overall yield of 63% from 48 (Scheme 6). Finally, de-O-isopropylidenation of 51 gave the desired diol 52.

Selective protection of hydroxyls in 52 by sequential silylation with TBSCl-ImH (-> 53) and alkylation with BOMCl-*i*-$Pr_2NEt$ afforded 54 which was then conventionally converted, in four steps, into aldehyde 58.

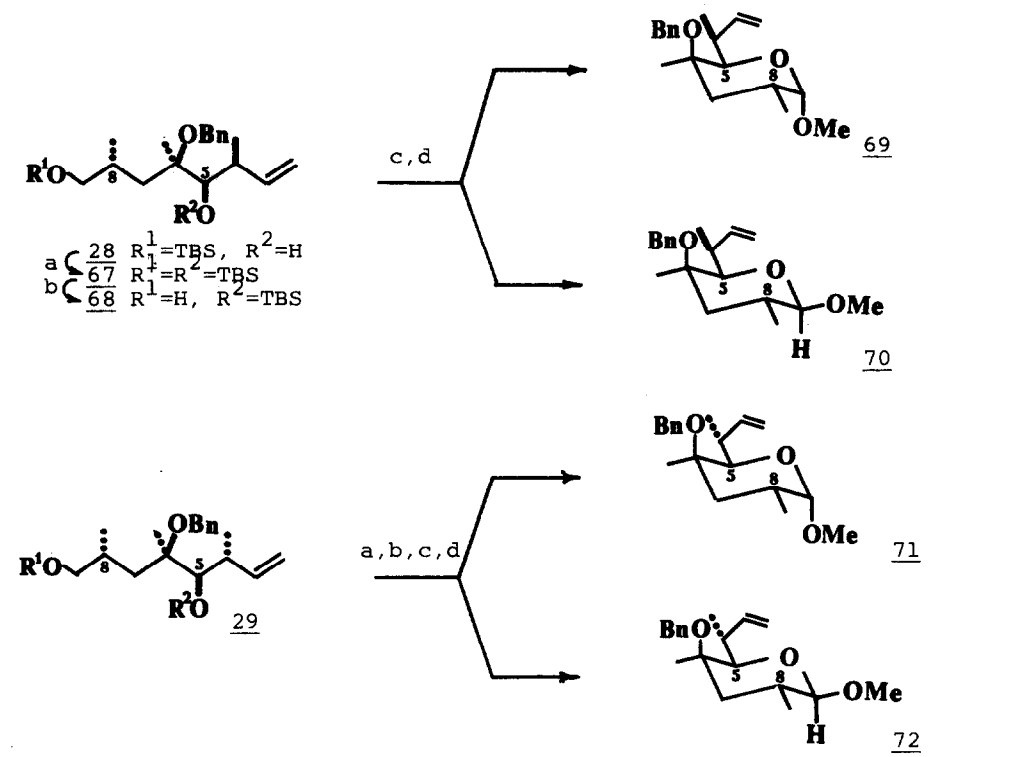
Preparation of the aldehyde 63 involved treatment of the diol 52 with *p*-methoxybenzylmethyl ether and DDQ[18] to give cyclic acetal 59 followed by conventional transformation steps. The "endo"-orientation of the aryl substituent in derivatives 59-63 followed from comparison of the chemical shift values for $H_{acetal}$ in $^1$H-NMR spectrum of 62 (δ 5.88) and the "exo"-acetal 64 (δ 6.08) (cf. [19]), the latter being formed from 62 in the presence of traces of acid.

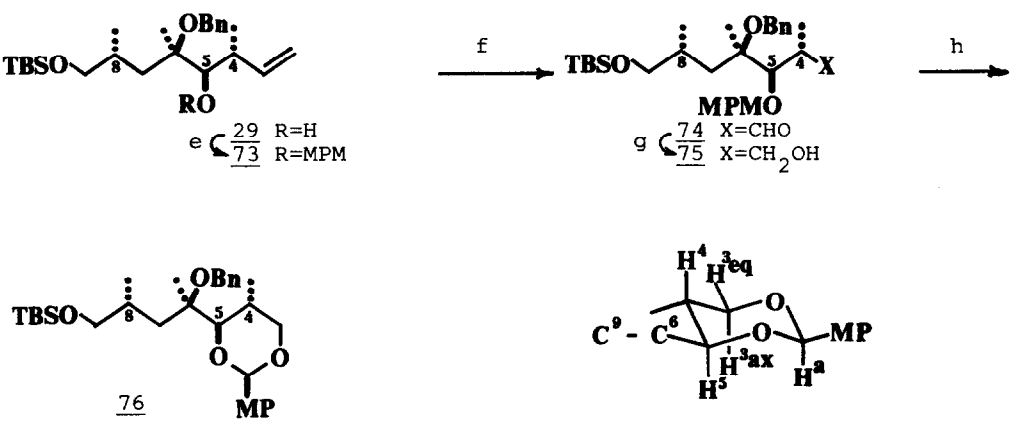
The third member of the series, aldehyde 66, was prepared from the known[6] dimethyl acetal 65 by hydrolysis.

4. Structural Elucidation of Addition Products of tri-*n*-butylcrotyl tin to the Aldehyde 27.

Configuration at C5 in addition products 28 and 29 was established on the basis of $^1$H-NMR data for the derived methyl glycosides 69, 70 and 71, 72

Scheme 7







a: TBSOTf, $Et_3N/CH_2Cl_2$, 98%; b: AcOH-$H_2O$-THF (6:1:3), 77%; c: $(COCl)_2$, DMSO, $Et_3N/CH_2Cl_2$, -60°; d: 3% HCl-MeOH, (c,d 73%); e: NaH, MPMCl/DMF, 97%; f: $O_3/CH_2Cl_2$-1% Py, -78°, 75%; g: $LiAlH_4/Et_2O$, -50°, 100%; h: DDQ MS 3A/$CH_2Cl_2$, 88%.

(Scheme 7). Silylation of the secondary hydroxyl in 28 to give 67 and selective hydrolytic removal of TBS-protective group from the primary hydroxyl (AcOH - $H_2O$ - THF) afforded 68. This was subjected to oxidation followed by methanolysis of an intermediate aldehyde (3% methanolic hydrogen chloride) to produce anomeric methyl glycosides 69 and 70 separated by chromatography. The same reaction sequence when applied to 29 resulted in glycosides 71 and 72.

Spectral data indicate the $^4C_1$ conformation for glycosides 69 and 70: $J_{1,2}$ being equal to 3.25 and 8 Hz, and $J_{2,3ax}$ 12.5 and 12 Hz, respectively, H1 being equatorial in 69 and axial in 70. That H5 in 70 possesses D-configuration followed from n.O.e at H1 upon pre-irradiation of H5 that corresponds to the "natural" configuration of this centre in the parent homoallylic alcohol 28. No n.O.e. for H1 and H5 protons was observed in the case of α-anomer 69. Analogous spectral features were characteristic of the glycosides 71 and 72 thus indicating D-configuration at C5 for the minor homoallylic alcohol 29.

To ascertain configuration at C4 in 29 this was converted, in a four-stage sequence, into the cyclic acetal 76 (Scheme 7). The coupling constant value ($J_{4,5}$= 9.5 Hz) corresponds to diaxial arrangement of H4 and H5 and, hence, to "*anti*"-orientation of Me-4 and OH-5 in the parent alcohol 29. Thus, *syn* ("natural") configuration at C4 and C5 was ascribed to the major product of addition of tri-*n*-butylcrotyl tin to the aldehyde 27 and this was proved in subsequent transformations.

## EXPERIMENTAL

Melting points were measured in a capillary and are uncorrected. Specific rotations were measured with a JASCO DIP-360 polarimeter for solutions in chloroform unless otherwise stated. $^1$H-NMR spectra were recorded on a Bruker WM-250 instrument with samples in $CDCl_3$ unless otherwise stated. Signals in the $^1$H-NMR spectra were assigned by using sequential, selective spin-decoupling experiments performed by the difference mode. The carbon atom numbering in the $^1$H-NMR spectra corresponds to that in erythronolides except compounds 14-23 and 41-51 where carbohydrate numbering is used.

All reactions with air- and moisture-sensitive compounds were conducted under positive argon pressure in an oven- or flame-dried glassware connected and evacuated hot prior filling with argon.

Reactions were monitored by TLC on silica gel plates (Merck). The components were detected by spraying the plates with 5% $H_2SO_4$ in MeOH followed by heating to 200°C. Extractive work-up involved dilution of a reaction mixture with an appropriate solvent (normally $CHCl_3$ or $Et_2O$) and washing with either M HCl to remove basic concomitants or with $NaHCO_3$ solution to remove acidic

ones. Organic layer was washed successively with water and brine and dried by passing through a pad of anh. $Na_2SO_4$. Finally, the solutions were concentrated by rotary evaporation (bath temperature *ca.* 40°C).

Reaction mixtures were separated by medium pressure liquid chromatography on silica gel Silpearl (25-40 μm) in the isocratic mode. Detection was monitored by a Knauer 88.00 refractometer.

Solvents were distilled under argon from a proper drying agent ($CaH_2$, $LiAlH_4$).

Compound 14. A solution of 13 (0.4 g, 2.03 mmol) in DMF (5 ml) was stirred with NaH (0.97 g, 4.06 mmol) for 1.5 h, 4-methoxybenzyl chloride was added, and stirring was continued for 2.5 h. The excess of NaH was decomposed with MeOH. Extractive work-up followed by chromatography (hexane-ether 3:1) gave 14 (0.619 g, 95%), m.p. 37° (heptane-EtOAc, 10:1), $[\alpha]_D^{20}$ -32° (C 1.0); $^1$H-NMR: δ 5.3 (1H, d: 1.8Hz, H-4), 1.97 (1H, br.d., H-2), 3.29 (1H, m: 1.5, 1.5, 1.5 Hz, H-3), 3.38 (1H, br.s., H-4), 4.58 (1H, br.d., H-5), 4.12 (1H, dd: 1.25, 7 Hz, H-6), 3.78 (1H, dd: 6 Hz, H-6'), 4.45 d and 4.54 d (2H, AB-spectrum, MeOPhC<u>H</u>$_2$O-), 4.25, 5.2, 5.27, 5.9 (5H, m, C<u>H</u>$_2$=C<u>H</u>-C<u>H</u>$_2$O-), 1.06 (3H, d: 7 Hz, Me-2), 3.81 (3H, s, <u>Me</u>OPhCH$_2$O-), 6.88 and 7.26 (4H, two m, MeO<u>Ph</u>CH$_2$O-). Found: C, 67.12; H 7.47. Calcd. for $C_{18}H_{24}O_5$: C, 67.47; H, 7.55%.

Compound 15. To a solution of 14 (0.619 g, 1.93 mmol) in DMSO (4 ml) was added *t*-BuOK (0.27 g, 2.32 mmol), the mixture was stirred for 2 h, poured into water and extracted with $CHCl_3$. The solution was concentrated. The residue was dissolved in 9:1 acetone-water (30 ml) and $Hg(OAc)_2$ (0.619 g, 1.93 mmol) was added. The mixture was stirred for 10 min and evaporated. The residue was distributed between water and chloroform. The organic phase was successively washed with 10% KI solution, water, and brine. The solvent was evaporated and the residue was chromatographed (hexane-EtOAc 2:3) to give 15 (0.483 g, 90,6%) m.p.91.5°C, $[\alpha]_D^{20}$-41.8° (C 1.1); $^1$H-NMR: δ 5.31 (1H, br.s., H-1), 2.0 (1H, br.q., H-2), 3.3 (1H, m, H-3), 3.68 (1H, br.d., H-4), 4.5 (1H, m, H-5), 4.25 (1H, dd: 1.2, 7 Hz, H-6), 3.76 (1H, dd: 6.7 Hz, H-6'), 1.1 (3H, d: 7.5 Hz, Me-2), 3.81 (3H, s, <u>Me</u>OPhCH$_2$O-), 4.46 and 4.54 (2H, AB-spectrum, MeOPhC<u>H</u>$_2$O-), 6.8-7.2 (4H, m, MeO<u>Ph</u>CH$_2$O-). Found: C, 64.17, H, 7.36%. Calcd. for $C_{15}H_{20}O_5$ C, 64.26, H, 7.19%.

Compound 16. A solution of DMSO (3.51 ml, 49.56 mmol) in $CH_2Cl_2$ (5 ml) was added to a stirred solution of $(COCl)_2$ (3.14 ml, 24.78 mmol) in the same solvent at -60°C. After 10 minutes a solution of 15 (5.97 g, 20.65 mmol) in $CH_2Cl_2$ (30 ml) was added to the above mixture. The stirring was continued and after 25 minutes triethylamine (13.81 ml, 99.12 mmol) was added at the same

temperature. The reaction mixture was warmed to 0°C in 3 minutes and then M HCl (103 ml) was added. The layers were separated. The aqueous phase was extracted with 50 ml of $CHCl_3$. The usual extractive work-up followed by chromatography (hexane-EtOAc 4:1) gave 16 (5.56 g, 97%), m.p.81.5°C (ether), $[\alpha]_D^{20}$+76.1° (C 2.35). $^1$H-NMR: δ 5.35 (1H, s, H-1), 1.87 (1H, br.d., H-2), 3.81 (1H, br.d., H-3), 4.65 (1H, br.d., H-5), 3.96 (1H, d: 7 Hz, H-6), 3.72 (1H, dd: 5, 7 Hz, H-6'), 1.2 (3H, d, Me-2), 3.81 (3H, s, MeOPhCH$_2$O-), 4.42 d and 4.86 d (2H, AB-spectrum, MeOPhCH$_2$O-), 6.89 m and 6.31 m (4H, MeOPhCH$_2$O-). Found: C, 64.89%; H, 6.81%. Calcd. for $C_{15}H_{18}O_5$ C, 64.73%; H, 6.51%.

Compound 17. A solution of 16 (5,12 g, 18.42 mmol) in THF (40 ml) was treated with 2 N MeMgBr solution in THF (11 ml) at -40°C. After 10 minutes the reaction mixture was warmed to room temperature. A saturated $NH_4Cl$ solution was added dropwise until crystalline precipitate was formed. The latter was separated and washed with ether. The filtrate and washings were combined and concentrated. The residue was crystallized from hexane to give 17 (5.31 g, 98%), m.p.64.4°C, $[\alpha]_D^{20}$-85.3° (C 0.75); $^1$H-NMR: δ 5.25 (1H, br.s., H-1), 2.21 (1H, m, H-2), 3.72 (1H, s, H-3), 4.02 (1H, br.d., H-5), 4.32 (1H, d: 7.5 Hz, H-6), 3.63 (1H, dd: 7.5, 5.5 Hz, H-6'), 1.08 (3H, d: 7.5 Hz, Me-2), 4.32 d and 4.65 d (2H, AB-spectrum, MeOPhCH$_2$O-), 3.8 (3H, s, MeOPhCH$_2$O-), 6.9 m and 7.26 m (4H, MeOPhCH$_2$O-). Found: C, 65.23%; H, 7.64%. Calcd. for $C_{16}H_{22}O_6$ C, 65.28%; H, 7.53%.

Compound 18. A solution of 17 (0.526 g, 1.78 mmol) in DMF (5 ml) was stirred with NaH (0.085 g, 3.56 mmol) for 1.5 h. Benzyl bromide (0.364 g, 2.136 mmol) was added at +10°C. Stirring was continued for 2 hrs. The excess of NaH was decomposed with MeOH. Usual work-up followed by chromatography (hexane-EtOAc 4:1) gave 18 (0.636 g, 93%), syrup, $[\alpha]_D^{20}$-22.7° (C 4.15); $^1$H-NMR: δ 5.38 (1H, br.s., H-1), 2.37 (1H, br.q., H-2), 3.43 (1H, br.s., H-3), 4.21 (1H, br.d., H-5), 4.79 (1H, d: 6.7 Hz, H-6), 3.73 (1H, dd: 6.7, 5.5 Hz, H-6'), 1.2 (3H, d: 8 Hz, Me-2), 1.61 (3H, s, Me-4), 3.88 (3H, s, MeOPhCH$_2$O-), 4.4 d and 4.7 d (2H, AB-spectrum, MeOPhCH$_2$O-), 4.5 (2H, m, AB-spectrum, PhCH$_2$O-), 6.9, 7.35 (9H, m, MeOPhCH$_2$O-, PhCH$_2$O-).

Compound 19. To a stirred solution of 18 (0.384 g, 0.998 mmol) in wet $CH_2Cl_2$ (13 ml) DDQ (0.45 g, 1.98 mmol) was added. After 20 minutes the reaction mixture was filtered through celite. The filtrate was washed successively with 5% $NaHCO_3$ (2 x 20 ml), water, and brine. The solvent was removed *in vacuo*. The residue was chromatographed (hexane-EtOAc 3:2) to give 19 (0.224 g, 85%), $[\alpha]_D^{20}$ -14.7° (C 6.7); $^1$H-NMR: δ 5.3 (1H, br.s., H-1), 2.19 (1H, br.q., H-2), 3.57 (1H, m, H-3), 4.24 (1H, br.d., H-5), 4.42 (1H, d: 7.6 Hz, H-6), 3.64 (1H, dd: 7.6, 5.5 Hz, H-6'), 1.11 (3H, d: 7.5 Hz, Me-2), 1.56 (3H,

s, Me-4), 4.5 d and 4.64 d (2H, AB-spectrum, $PhC\underline{H}_2O$-), 7.35 (5H, m, $\underline{Ph}CH_2O$-).

Compound 21. A solution of 19 (4.81 g, 18.2 mmol) in THF (80 ml) was stirred with NaH (0.873 g, 36.4 mmol) and imidazole (0.02 g) for 1 h. Carbon disulfide (2.2 ml, 36.4 mmol) was added followed after 20 minutes by the addition of methyl iodide (2.26 ml, 36.4 mmol). Stirring was continued for additional 1 h. The excess of NaH was decomposed with MeOH. The solution was concentrated *in vacuo*. Water was added to the residue. The usual extractive work-up yielded the desired xanthate ester. The later was dissolved in toluene (50 ml) and $Bu_3SnH$ (5.4 ml, 20 mmol) was added to this solution. The reaction was initiated by the addition of several drops of saturated AIBN/toluene solution to the boiling xanthate/ $Bu_3SnH$ solution. Boiling was continued for additional 2 hrs. The solvent was removed *in vacuo* and the residue was chromatographed (hexane→hexane:ether 2:1) to give 21 (3.88 g, 86%), $[\alpha]_D^{20}$-16.6° (C 1.2); $^1$H-NMR: δ 5.24 (1H, s, H-1), 1.98 (1H, m, H-2), 2.11 (1H, dd: 13, 7.2 Hz, H-3), 1.62 (1H, br.d., H-3´), 4.18 (1H, br.d., H-5), 4.37 (1H, d: 7.2 Hz, H-6), 3.69 (1H, dd: 7.2, 5 Hz, H-6´), 1.1 (3H, d: 7.2 Hz, Me-2), 1.6 (3H, s, Me-4), 4.42 d and 4.52 d (2H, AB-spectrum, $PhC\underline{H}_2O$-), 7.33 (5H, m, $\underline{Ph}CH_2O$-).

Compound 22. Compound 21 (5.4 g, 21.75 mmol) was dissolved in MeOH containing 5% w/w HCl (100 ml) and the reaction mixture was kept at room temperature for 12 hrs. Acid was neutralyzed with 5% $NaHCO_3$ solution and after extractive work-up crude 22 (6 g, ~100%) was obtained as a mixture of anomers. Separation of 120 mg of the above mixture (hexane-EtOAc 1:1) gave α-22 (85 mg, 70%) and β-22 (35 mg, 30%), α-22: $[\alpha]_D^{20}$+91° (C 1.2), $^1$H-NMR: δ 4.61 (1H, d: 3.5 Hz, H-1), 2.15 (1H, m, H-2), 1.89 (1H, dd: 14.5, 4 Hz, H-3), 1.49 (1H, dd: 14.5, 13 Hz, H-3´), 3.59 (1H, dd: 5.5, 3 Hz, H-5), 4.7 (1H, dd: 11.5, 1.2 Hz, H-6), 3.77 (1H, m, H-6´), 2.9 (1H, br.d., OH-6), 0.9 (3H, d: 7 Hz, Me-2), 1.26 (3H, s, Me-4), 3.38 (3H, s, MeO-), 4.42 (2H, AB-spectrum, $PhC\underline{H}_2O$-), 7.3 (5H, m, $\underline{Ph}CH_2O$-).

Compound 23. To a solution of 22 (nonseparated mixture) (0.64 g, 2.28 mmol) in pyridine (10 ml) were added $PPh_3$ (1.19 g, 4.56 mmol) and $CBr_4$ (1.54 g, 4.56 mmol). The reaction was kept for 3 hrs at +60°C. Addition of MeOH (1 ml) followed by extractive work-up and chromarography (hexane-ether 9:1) gave 23 (0.757 g, 96%). For α-anomer: $[\alpha]_D^{20}$+95.2° (C 1.2); $^1$H-NMR: δ 6.1 (1H, d: 3.2 Hz, H-1), 2.12 (1H, m, H-2), 1.88 (1H, dd: 8, 14 Hz, H-3), 1.5 (1H, dd: 14, 13 Hz, H-3´), 3.81 (1H, m, H-5), 3.7 (2H, m, H-6, H-6´), 3.48 (3H, s, MeO-), 1.22 (3H, s, Me-4), 0.9 (3H, d: 7 Hz, Me-2), 4.42 (2H, AB-spectrum, $PhC\underline{H}_2O$-), 7.32 (5H, m, $\underline{Ph}CH_2O$-).

Compound 26. A solution of 23 (mixture of anomers) (0.245 g, 0.7 mmol)

in 14:1 *i*-PrOH:$H_2O$ (8 ml) was refluxed for 1 h with activated Zn-dust (2.33 g, 35.6 mmol). The reaction mixture was filtered through a pad of celite; the filtrate was diluted with water (50 ml) and extracted with ether (3 x 10 ml). The usual extractive work-up gave crude 24 (0.158 g, 96%). This was dissolved in ether (2 ml) and treated with $LiAlH_4$ (0.25 ml, N soln. in THF) at -50°C for 30 min. The reaction mixture was warmed to room temperature and an excess of $Na_2SO_4.10H_2O$ was added. This suspension was stirred for 1 h, filtered through a pad of anh. $Na_2SO_4$ and the solvent was removed *in vacuo*. The residue (crude 25) (0.148 g, 92%) was dissolved in DMF (1 ml), TBSCl (0.19 g, 1.26 mmol) and imidazole (0.17 g, 2.52 mmol) were added and the reaction mixture was kept at +25°C for 12 hrs. The usual extractive work-up followed by chromatography (hexane-ether 80:1) gave 26 (0.2 g, 80% based on 23), $[\alpha]_D^{23}$-9.8° (C 1.0); $^1$H-NMR: δ 0.025 (6H, s, *t*BuMe$_2$SiO-), 0.9 (9H, s, *t*BuMe$_2$SiO-), 0.98 (3H, d: 8.5 Hz, Me-8), 1.38 (3H, s, Me-6), 7.4 (1H, dd: 13.5, 4 Hz, H-7), 1.76 (1H, dd: 13.5, 4.5 Hz, H-7´), 1.84 (1H, m, H-8), 3.34 (1H, dd: 9, 6.5 Hz, H-9), 3.53 (1H, dd; 9, 5.7 Hz, H-9´), 4.4 (2H, Ab-spectrum, PhCH$_2$O-), 5.23 (2H, m, CH$_2$=CH-), 5.9 (1H, m, CH$_2$=CH-), 7.34 (5H, m, PhCH$_2$O-).

Compound 27. A solution of 26 (0.307 g, 0.88 mmol) in $CH_2Cl_2$ (65 ml) was ozonized at -78°C in the presence of pyridine (1 ml) and Sudan IV (1 ml of 0.05% soln) until discolouration occured. The reaction mixture was treated with an excess of $Me_2S$ and slowly warmed to +25°C in 1 h. The solvent was removed *in vacuo*, the residue was evaporated twice with heptane to remove pyridine, and its solution in $CHCl_3$ passed through a pad of $SiO_2$. Finally, pure 27 was obtained by chromatography (hexane-ether 96:4) (0.264 g, 86%), $[\alpha]_D^{20}$+19° (C 1.0); $^1$H-NMR: δ 0.05 (6H, s, *t*BuMe$_2$SiO-), 0.9 (9H, s, *t*BuMe$_2$SiO-), 0.96 (3H, d: 6.5 Hz, Me-8), 1.38 (3H, s, Me-6), 1.5 (1H, dd: 13.5 Hz, H-7), 1.92 (2H, m, H-7´, H-8), 3.66 (1H, dd: 9.5, 5.7 Hz, H-9), 4.6 (1H, dd: 5.5 Hz, H-9´), 4.5 (2H, AB-spectrum. PhCH$_2$O-), 7.36 (5H, m, PhCH$_2$O-), 9.65 (1H, s, aldehydic proton).

Compounds 28 and 29. To a stirred suspension of $MgBr_2$ (0.508 g, 2.76 mmol) in $CH_2Cl_2$ (3 ml) a solution of 27 (0.82 g, 2.3 mmol) in $CH_2Cl_2$ (3 ml), and neat tri-*n*-butylcrotyl tin (1 ml, 2.54 mmol) were added successively in a period of 5 min. The reaction mixture was stirred at +25°C for 50 hrs, diluted with water, and extracted with $CHCl_3$. The usual work-up followed by chromatography (hexane-ether 95:5) gave 28 (0.6 g, 64%) and 29 (0.14 g, 16%). 28: $[\alpha]_D^{20}$+8.6° (C 0.5), $^1$H-NMR: δ 0.06 (6H, s, *t*BuMe$_2$SiO-), 0.93 (9H, s, *t*BuMe$_2$SiO-), 1.01 (3H, d: 6.5 Hz, Me-4), 1.14 (3H, d: 6.5 Hz, Me-8), 1.3 (3H, s, Me-6), 1.55 (1H, dd: 14.5, 7.5 Hz, H-7), 1.85 (1H, dd: 14.5, 3.2 Hz, H-

7'), 1.9 (1H, m, H-8), 2.45 (1H, m, H-4), 3.4 (2H, AB-spectrum, H-9, H-9'), 3.63 (1H, d: 5 Hz, H-5), 4.5 (2H, AB-spectrum, $PhC\underline{H}_2O$-), 4.99 and 5.4 (2H, m, $C\underline{H}_2$=CH-), 5.9 (1H, m, $CH_2$=C<u>H</u>-), 7.35 (5H, m, <u>Ph</u>$CH_2O$-). <u>29</u>: $[\alpha]_D^{20}$+5.4° (C 4.85): $^1$H-NMR: δ 0.05 (6H, s, *t*Bu<u>Me</u>$_2$SiO-), 0.9 (9H, s, *t*<u>Bu</u>Me$_2$SiO-), 0.99 (3H, d: 6.5 Hz, Me-8), 1.19 (3H, d: 7 Hz, Me-4), 1.27 (3H, s, Me-6), 1.43 (1H, dd: 15.5, 8.5 Hz, H-7), 1.83 (1H, dd: 15.5, 3.2 Hz, H-7'), 1.85 (1H, m, H-8), 2.51 (2H, m, H-4, OH), 3.39 m and 3.43 m (2H, H-9, H-9'), 4.63 (1H, br.s., H-5), 4.46 (2H, AB-spectrum, $PhC\underline{H}_2O$-), 5.02 (2H, m, $C\underline{H}_2$=CH-), 6.06 (1H, m, $CH_2$=C<u>H</u>-), 7.35 (5H, m, <u>Ph</u>$CH_2O$-).

Compound <u>30</u>. A solution of <u>28</u> (0.6 g, 1.48 mmol) in DMF (3 ml) was stirred with NaH (0.07 g, ~3 mmol) at +25°C for 1 h. 4-Methoxybenzyl chloride (0.43 ml, 3 mmol) was added and the reaction mixture was left overnight. An excess of NaH was decomposed with MeOH. The usual extractive work-up followed by chromatography (hexane-ether 96:4) gave <u>30</u> (0.76 g, 97%), $[\alpha]_D^{20}$-29° (C 1.0); $^1$H-NMR: δ 0.0 (6H, s, *t*Bu<u>Me</u>$_2$SiO-), 0.88 (9H, s, *t*<u>Bu</u>Me$_2$SiO-), 0.99 (3H, d: 6.7 Hz, Me-4), 1.15 (3H, d: 7 Hz, Me-8), 1.36 (3H, s, Me-6), 1.45 (1H, dd: 14.5, 6 Hz, H-7), 1.7 (1H, dd: 14.5, 5.5 Hz, H-7'), 1.92 (1H, m, H-8), 2.74 (1H, m, H-4), 3.28 (1H, dd: 9.7, 7.5 Hz, H-9), 3.55 (1H, d: 3 Hz, H-5), 2.62 (1H, dd: 9.7, 5.5 Hz, H-9'), 3.83 (3H, s, <u>Me</u>O$PhCH_2O$-), 4.5 (2H, AB-spectrum), 4.57 (2H, AB-spectrum), 4.93 m and 5.0 (2H, $C\underline{H}_2$=CH-), 5.98 (1H, m, $CH_2$=C<u>H</u>-), 6.9 and 7.3 (9H, m, <u>Ph</u>$CH_2O$-, MeO<u>Ph</u>$CH_2O$-).

Compound <u>31</u>. To a solution of <u>30</u> (1 g, 1.78 mmol) and NMO-monohydrate (0.513 g, 3.8 mmol) in 8:1 acetone-water (5 ml) was added $OsO_4$ (0.024 g, 0.095 mmol). The reaction mixture was kept at +25°C for 12 hrs. A solution of $K_2S_2O_5$ was added and stirring was continued for 1 h. The usual work-up yielded crude dihydroxyl derivative which was dissolved in 6:1 THF-water (6 ml) and treated with $NaIO_4$ (0.45 g, 2 mmol). Extractive work-up followed by chromatography (hexane-ether 85:15) gave <u>31</u> (0.92 g, 92%), $[\alpha]_D^{20}$ -27.6° (C 0.5); $^1$H-NMR: δ 0.01 (6H, s, *t*Bu<u>Me</u>$_2$SiO-), 0.88 (9H, s, *t*<u>Bu</u>Me$_2$SiO-), 0.98 (3H, d: 6.6 Hz, Me-8), 1.26 (3H, d: 7 Hz, Me-4), 1.4 (3H, s, Me-6), 1.49 (1H, dd: 15, 5.5 Hz, H-7), 1.63 (1H, dd: 15, 6 Hz, H-7'), 1.91 (1H, m, H-8), 2.92 (1H, m, H-4), 3.26 (1H, dd: 9.6, 1.5 Hz, H-9), 3.63 (1H, dd: 9.6, 5.5 Hz, H-9'), 3.82 (3H, s, <u>Me</u>O$PhCH_2O$-), 4.05 (1H, d: 3.9 Hz, H-5), 4.45 (4H, two AB-spectra, $PhC\underline{H}_2O$-, MeO$PhC\underline{H}_2O$-), 6.9, 7.3 (9H, m, <u>Ph</u>$CH_2O$-, MeO<u>Ph</u>$CH_2O$-), 9.64 (1H, d: 1.5 Hz, aldehydic proton).

Compound <u>32</u>. To a stirred solution of <u>31</u> (0.097 g, 0.18 mmol) in $CH_2Cl_2$ (1 ml) at -78°C $BF_3$·$Et_2O$ (0.034 ml, 0.275 mmol) was added followed after 5 minutes by tri-*n*-butylcrotyl tin (0.16 ml, 0.4 mmol). Stirring was continued for 45 min, then an excess of sat. $NH_4Cl$ soln was added at the same tempera-

ture. Extractive work-up followed by chromatography (hexane-ether 4:1) gave 32 (0.078 g, 72%), $[\alpha]_D^{20}$-6° (C 0.25); $^1$H-NMR: δ 0.035 (6H, s, *t*BuMe$_2$SiO-), 0.9 (9H, s, *t*BuMe$_2$SiO-), 0.96 (3H, d: 6.7 Hz, Me-8), 1.0 (3H, d: 6.5 Hz, Me-2), 1.04 (3H, d: 6.7 Hz, Me-4), 1.4 (3H, s, Me-6), 1.44 (1H, dd: 15, 6.7 Hz, H-7), 1.68 (1H, dd: 15, 4 Hz, H-7´), 1.87 (1H, m, H-8), 2.15 (1H, m, H-4), 2.28 (1H, m, H-2), 3.33 (1H, dd: 9.5, 6.7 Hz, H-9), 3.5 (1H, dd: 9.5, 6 Hz, H-9´), 3.47 (1H, br.d., H-3), 3.69 (1H, d: 3.5 Hz, H-5), 3.8 (3H, s, MeOPhCH$_2$O-), 4.53 (2H, s, A$^2$-spectrum), 4.61 d and 4.82 d (2H, AB-spectrum), 4.96 m and 5.04 m (2H, CH$_2$=CH-), 5.57 (1H, m, CH$_2$=CH-), 6.87, 7.3 (9H, m, PhCH$_2$O-, MeOPhCH$_2$O-).

Compound 33. To a stirred solution of 32 (0.078 g, 0.13 mmol) in $CH_2Cl_2$ (1 ml) powdered molecular sieves 3A (0.1 g) and DDQ (0.033 g, 0.14 mmol) were added. Stirring was continued for 30 min at +25°C. Then sat. $Na_2SO_3$ soln. was added and the reaction mixture was filtered through a pad of celite. The filtrate was washed with sat. $NaHCO_3$ soln. The usual extractive work-up followed by chromatography (hexane-ether 95:5) gave 33 (0.063 g, 81%), $[\alpha]_D^{20}$ -14.8° (C 2.0); $^1$H-NMR: δ 0.01 (6H, s, *t*BuMe$_2$SiO-), 0.94 (9H, s, *t*BuMe$_2$SiO-), 1.07 (1H, d: 6.6 Hz, Me-8), 1.18 (6H, two d, Me-4, Me-2), 1.4 (3H, s, Me-6), 1.4 (1H, dd: 15, 7.5 Hz, H-7), 1.94 (3H, m, H-4, H-8, H-7´), 2.54 (1H, m, H-2), 3.88 (1H, dd: 10, 7 Hz, H-9), 3.45 (1H, dd: 10, 2 Hz, H-3), 3.56 (1H, dd: 10, 6 Hz, H-9´), 3.89 (1H, d: 2 Hz, H-5), 3.5 (3H, s, MeOPhCH<), 4.74 (2H, AB-spectrum, PhCH$_2$O-), 5.1 and 5.19 (2H, m, CH$_2$=CH-), 5.47 (1H, s, MeOPhCH<), 6.95 and 7.3 (9H, m, PhCH$_2$O-. MeOPhCH<). nOe: $[H_A]$, $H^5$ = 6.5%; $[H_A]$, $H^3$ = 7.5%.

Compound 34. A solution of 33 (0.205 g, 0.35 mmol) and TsOH·$H_2O$ (0.066 g, 0.35 mmol) in 1:1 DMP:acetone was kept at +25°C for 12 hrs. The usual work-up followed by chromatography (hexane-EtOAc 88:12) gave 34 (0.13 g, 95%), $[\alpha]_D^{20}$+16° (C 4.75). $^1$H-NMR: δ 0.93 (3H, d: 6 Hz, Me-4), 0.96 (3H, d: 6.8 Hz, Me-8), 1.05 (3H, d: 6.5 Hz, Me-2), 1.34 (1H, dd: 14.5, 11 Hz, H-7), 1.4, 1.42, 1.45 (9H, three s, Me-6, Me-groups of the isopropylidene moiety), 1.65 (1H, m, H-4), 1.71 (1H, dd, H-7´), 2.0 (1H, m, H-8), 2.32 (1H, m, H-2), 3.25 (1H, m, H-9), 3.45 (1H, dd: 2, 10 Hz, H-3), 5.25 (1H, m, H-9´), 3.99 (1H, d: 2 Hz, H-5), 4.6 d and 4.74 d (2H, AB-spectrum, PhCH$_2$O-), 5.00, 5.11 (2H, m, CH$_2$=CH-), 5.59 (1H, m, CH$_2$=CH-), 7.3 (5H, m, PhCH$_2$O-).

Compound 6. Primary alcohol 34 (0.13 g) was oxidized followed the standard Swern procedure[20]. The crude aldehyde 35 (0.13 g) was treated with an excess of EtMgBr in THF at -50°C to give epimeric secondary alcohols 36 (0.15 g). These were oxidized in the same conditions to yield after chromatographic purification (hexane-ether 9:1) 6 (0.108 g, 78% based on 34), $[\alpha]_D^{20}$+22.3° (C

1.0); $^1$H-NMR: δ 0.66 (3H, t, Me-10), 0.94 (3H, d: 7 Hz, Me-4), 1.03 (3H, d: 6.5 Hz, Me-2), 1.06 (3H, d: 7 Hz, Me-8), 1.27 (1H, dd: 14, 2.5 Hz, H-7), 1.35, 1.42 (9H, three s, Me-6, Me-groups of the isopropylidene moiety), 1.66 (1H, m, H-4), 2.12 (1H, m, H-10), 2.33 (3H, m, H-10', H-7', H-2), 2.8 (1H, m, H-8), 3.44 (1H, dd: 2, 10 Hz, H-3), 3.92 (1H, d: 2 Hz, H-5), 4.47 d and 4.6 d (2H, AB-spectrum, PhC$\underline{H}_2$O-), 5.05, 5.1 (2H, m, C$\underline{H}_2$=CH-), 5.6 (1H, m, CH$_2$=C$\underline{H}$-), 7.25 (5H, m, $\underline{Ph}$CH$_2$O-).

Compound 38. To a solution of 37 (1.31 g, 7.01 mmol) and $Et_3N$ (1.95 ml, 11.5 mmol) in $CH_2Cl_2$ (10 ml) tert-butyldimethylsilyl trifluoromethanesulfonate (1.95 ml, 8.4 mmol) was added at -78°C. The reaction mixture was stirred for 20 min, warmed to ambient temperature and quenched with sat. $NaHCO_3$ soln. (5 ml). Extractive work-up followed by chromatography (hexane-ether 95:5) gave 38 (1.76 g, 83%), $[\alpha]_D^{20}$ -0.6° (C 0.4); $^1$H-NMR: δ 0.06 (6H, two s, *t*Bu$\underline{Me}_2$SiO-), 0.74 (3H, d: 6.7 Hz, Me-12), 0.83 (3H, t, Me-14), 0.89 (9H, s, *t*$\underline{Bu}$Me$_2$SiO-), 1.34, 1.39 (6H, two s, Me-groups of the isopropylidene moiety), 1.48 (2H, m, H-14, H-14'), 1.65 (1H, m, H-12), 3.55 (3H, m, H-10, H-10'. H-11), 3.87 (1H, m, H-13).

Compound 39. To a solution of 38 (0.36 g. 1.19 mmol) and 1,3-propanedithiol (0.238 ml, 2.38 mmol) in $CH_2Cl_2$ (6 ml) was added $BF_3 \cdot Et_2O$ (0.292 ml, 2.38 mmol) at -78°C. The reaction mixture was stirred for 1 h and quenched with sat. $NaHCO_3$ soln. at the same temperature. Extractive work-up followed by chromatography (hexane-EtOAc 7:3) gave 39 (0.24 g, 77%); $[\alpha]_D^{20}$ +20.6° (C 1.0); $^1$H-NMR: δ 0.1, 0.14 (6H, two s, *t*Bu$\underline{Me}_2$SiO-), 0.8 (3H, d: 7 Hz, Me-12), 0.92 (9H, s, *t*$\underline{Bu}$Me$_2$SiO-), 0.96 (3H, t, Me-14), 1.57 (2H, H-14, H-14'), 1.98 (1H, m, H-12), 3.5, 3.7 (4h, m, H-10, H-10', H-11, H-13).

Compound 40. To a solution of 39 (0.14 g, 0.53 mmol) in 4:1 THF-water (5 ml) was added finely powdered $NaIO_4$ (0.456g, 2.14 mmol) in two portions in a 10 minutes period. After additional 10 min the reaction mixture was diluted with ether (2 ml) and filtered through a pad of celite, the filter cake was washed with ether (10 ml). Evaporation of the combined filtrates followed by chromatography (hexane-ether 50:1) gave 40 (0.103 g, 84%), $[\alpha]_D^{28}$ +62° (C 1.0); $^1$H-NMR: δ 0.05, 0.075 (6H, two s, *t*Bu$\underline{Me}_2$SiO-), 0.88 (3H, t, Me-14), 0.87 (9H, s, *t*$\underline{Bu}$Me$_2$SiO-), 1.07 (3H, d: 7 Hz, Me-12), 1.53 (2H, m, H-14, H-14'), 2.47 (1H, m, H-13), 9.77 (1H, d: 0.75 Hz, aldehydic proton).

Compound 41. To a refluxed suspension of $LiAlH_4$ (2.03 g, 53.5 mmol) in THF (100 ml) was added dropwise a solution of 12 (8.9 g, 48.5 ml) in THF (50 ml) in 30 minutes. Reflux was continued for additional 2 h. The reaction mixture was cooled to ambient temperature and quenched by successive addition of water (2 ml), 15% NaOH soln. (2 ml), and again water (6 ml). The precipitate

was separated by filtration. The filtrate was evaporated to yield 41 (8.99 g, 99%), $[\alpha]_D^{27}$-77.2° (C 2.9), $^1$H-NMR: δ 5.03 (1H, s, H-1), 1.73 (1H, d: 15 Hz, H-2), 2.08 (1H, ddd: 5.05 Hz, H-3), 3.8 (1H, br.d., H-3´), 3.3 (1H, br.s, H-4), 4.53 (1H, br.d., H-5), 3.65 (1H, dd: 7.5, 5.05 Hz, H-6), 4.15 (1H, d, H-6´), 4.07 d, 5.2 br.dd., and 5.7 m (5H, $C\underline{H}_2$=C$\underline{H}$-C$\underline{H}_2$O-).

Compound 42. A solution of 41 (1.53 g, 8.2 mmol), *i*-$Pr_2$NEt (3.48 ml, 20 mmol), and BOM-Cl (2.5 ml, 18 mmol) was kept for 48 hrs at ambient temperature. The reaction mixture was quenched with M HCl (20 ml) and extracted with $CHCl_3$. Usual work-up followed by chromatography (hexane-EtOAc 55:45) gave 42 (2.27 g, 90%), $[\alpha]_D^{26}$ -44.2° (C 1.0), $^1$H-NMR: δ 5.57 (1H, s, H-1), 1.86 (1H, br.d: 15 Hz, H-2), 2.08 (1H, ddd: 6, 2, 15 Hz, H-2´), 3.91 (1H, m, H-3), 3.4 (1H, br.s., H-4), 4.58 (1H, m, H-5), 3.75 (1H, dd: 7, 6 Hz, H-6), 4.20 (1H, dd; H-6´), 4.10, 5.23, 5.9 (5H, $C\underline{H}_2$=C$\underline{H}$-C$\underline{H}_2$O-), 4.63 (2H, AB-spectrum), 4.86 (2H, $A^2$-spectrum), 7.35 (5H, m, $\underline{Ph}CH_2$O-).

Compound 43. To a solution of 42 (2.27 g, 7.4 mmol) in DMSO (20 ml) was added *t*-BuOK (0.99 g, 8.8 mmol). The reaction mixture was stirred for 1 h at +60°C and then quenched with solid $CO_2$ and water (5 ml). The bulk of DMSO was removed by distillation *in vacuo*. The residue was dissolved in water and extracted with $CHCl_3$ (2 x 30 ml). The combined organic phases were concentrated, the residue was dissolved in 10:1 acetone-water (30 ml) and $Hg(OAc)_2$ (2.68 g, 8.4 mmol) was added to the stirred solution. After 10 minutes the reaction mixture was evaporated, the residue was suspended in water and extracted with EtOAc (3 x 30 ml). The combined organic phases were washed successively with 10% KI soln., water, and brine. Charcoal was added and the solution was filtered and concentrated. The residue was flash-chromatographed on silica with hexane-EtOAc 1:1 to give 43 (1.74 g, 88%), $[\alpha]_D^{27}$-27.4° (C 1.0), $^1$H-NMR: δ 5.55 (1H, s, H-1), 1.86 (1H, br.d., H-2), 2.06 (1H, ddd:15, 2 Hz, H-2´), 3.89 (1H, br.d., H-3), 3.7 (1H, s, H-4), 4.5 (1H, br.d., H-5), 3.77 (1H, dd: 6, 6 Hz, H-6), 4.82 (1H, d, H-6´), 4.82 and 4.64 (4H, two AB-spectra, PhC$\underline{H}_2$OC$\underline{H}_2$O-), 7.3 (5H, m, $\underline{Ph}CH_2OCH_2$O-).

Compound 45. This was prepared starting from 43 in 89% overall yield according to the procedure described for the preparation of compounds 16 and 17. The intermediate ketone 44 was not purified and was directly treated with MeMgBr. $[\alpha]_D^{25}$-125° (C 1.0), $^1$H-NMR: δ 5.48 (1H, s, H-1), 1.9 (1H, ddd´ 15, 5, 2 Hz, H-2), 2.10 (1H, dd: 1.5, 1.5 Hz, H-2´), 3.6 (1H, dd, H-3), 3.63 (1H, s, H-4), 4.05 (1H, br.d., H-5), 3.64 (1H, dd: 7.5, 5.05 Hz, H-6), 4.32 (1H, d, H-6´), 1.4 (3H, s, Me-4), 4.64 dd and 4.83 dd (4H, two AB-spectra), 7.3 (5H, m, $\underline{Ph}CH_2$O-).

Compound 47. A solution of 45 (1.55 g, 5.5 mmol) in 5% w/w HCl-MeOH (20

ml) was kept at +25°C for 12 hrs. Acid was neutralyzed with solid $NaHCO_3$. The solution was filtered through a pad of celite and evaporated. The residue was diluted with $CHCl_3$ and filtered through a pad of anh. $Na_2SO_4$ and evaporated. The residue was dissolved in 1:1 acetone-DMP and camphorosulfonic acid (0.26 g) was added. The reaction mixture was kept for 3 hrs at +25°C and quenched with five drops of water followed after 5 minutes by an excess of $Et_3N$. The solution was evaporated and the usual extractive work-up followed by chromatography (EtOAc) gave 47 (0.873 g, 68% based on 45). $[\alpha]_D^{22}$+71.6° (C 1.0); $^1$H-NMR: δ 4.92 (1H, dd: 6, 7 Hz, H-1), 1.58 (1H, ddd: 2, 5, 15 Hz, H-2), 2.46 (1H, ddd: 3.25 Hz, H-2'), 4.09 (1H, ddd, H-3), 4.8 (1H, dd: 3.5, 6 Hz, H-5), 3.78 (1H, dd: 6 Hz, H-6), 3.94 (1H, dd, H-6'), 1.3, 1.36, 1.46 (9H, three s, Me-4 and Me-groups of the isopropylidene moiety), 3.42 (3H, s, OMe).

Compound 48. To a solution of 47 (1.28 g, 5.5 mmol) in HMPA (30 ml) were added $PPh_3$ (2.45 g, 9.35 mmol) and NBS (1.66 g, 9.35 mmol). The reaction mixture was heated at +80°C for 1 h, cooled, diluted with ether (30 ml), and washed with brine (4 x 20ml). Evaporation of the etheral solution followed by chromatography (hexane-ether 88:12) gave 48 (1.25 g, 77%), m.p. 65-65.5° sublimed, $[\alpha]_D^{24}$+113.2° (C 1.0); $^1$H-NMR (90 MHz): δ 4.9 (1H, dd: 7, 7 Hz, H-1), 1.55 (1H, ddd: 2.5, 15 Hz, H-2), 2.5 (1H, ddd: 3.5 Hz, H-2'), 4.1 (1H, dd, H-3), 3.53 (3H, m, H-5, H-6, H-6'), 1.27, 1.35, 1.43 (9H, three s, Me-4, Me-groups of the isopropylidene moiety), 3.5 (3H, s, -OMe).

Compound 51. 6-Bromoderivative 48 (0.448 g, 1.78 mmol) was treated with activated Zn-dust in boiling 14:1 *i*-PrOH-$H_2O$ and the thus prepared aldehyde 49 was reduced with $LiAlH_4$ in ether to give primary alcohol 50 following the protocol described for the preparation of compound 27. The crude 50 was dissolved in pyridine (5 ml) and benzoyl chloride (0.58 ml, 5 mmol) was added at 0°C. The reaction mixture was kept for 1 h at ambient temperature and quenched with M HCl (80 ml). The usual extractive work-up followed by chromatography (hexane-EtOAc 83:17) gave 51 (0.795 g, 73% based on 48), $[\alpha]_D^{27}$+9.8° (C 1.0); $^1$H-NMR: δ 1.92 (2H, m, H-14, H-14'), 3.9, 4.1, 5.2 (9H, three s, Me-12, Me-groups of the isopropylidene moiety), 4.2 (1H, dd: 5, 7.5 Hz, H-13), 4.45 (2H, m, H-15, H-15'), 5.2 (2H, m, $C\underline{H}_2$=CH-), 5.85 (1H, m, $CH_2$=C$\underline{H}$-), 7.45, 8.05 (5H, two m, Ph$\underline{C}$OO-).

Compound 53. A solution of 51 (0.445 g, 1.78 mmol) in 4:1:4 THF-$H_2O$-$CF_3COOH$ was kept for 5 hrs at +25°C. Acid was neutralyzed with solid $NaHCO_3$. The reaction mixture was diluted with water and extracted with $CHCl_3$. The usual extractive isolation yielded diol 52 (0.36 g, 83%) which was dissolved in DMF (3 ml) and treated with tert-butyldimethylsilyl chloride (0.43 g, 2.86 mmol) in the presence of imidazole (0.389 g, 5.72 mmol) for 12 hrs at

+55°C. The reaction mixture was quenched with M HCl and extracted with ether (2 x 30 ml). Extractive work-up followed by chromatography (hexane-ether 83:17) gave 53 (0.415 g, 80%), $[\alpha]_D^{29}$+6.7° (C 1.0); $^1$H-NMR (90 MHz): δ 0.18 (6H, s, *t*BuMe$_2$SiO-), 0.99 (9H, s. *t*BuMe$_2$SiO-), 1.3 (3H, s, Me-12), 2.0 (2H, m, H-14, H-14´), 3.75 (1H, dd, H-13), 4.44 (2H, m, H-15, H-15´), 5.3 (3H, m, CH$_2$=CH-), 7.5 and 8.0 (5H, m, PhCOO-).

Compound 54. A solution of 53 (0.415 g, 1.13 mmol), *i*-Pr$_2$NEt (0.98 ml, 5.64 mmol), and BOM-Cl (0.39 ml, 2.82 mmol) was kept for 60 hrs at +25°C. Since the reaction did not go to completion, the same amounts of reagents were added and the reaction mixture was kept for additional 48 hrs and quenched with M HCl (20 ml). Extractive work-up followed by chromatography (hexane-ether 9:1) gave 54 (0.492 g, 90%), $[\alpha]_D^{26}$+62.2° (C 1.0); $^1$H-NMR: δ 0.1 and 0.12 (6H, two s. *t*BuMe$_2$SiO-), 0.92 (9H, s, *t*BuMe$_2$SiO-), 1.4 (3H, s, Me-12), 1.9 and 2.13 (2H, two m, H-14, H-14´), 3.85 (1H, dd: 3.5, 9 Hz, H-13), 4.38 and 4.55 (2H, two m, H-15, H-15´), 4.65 and 4.82 (4H, two AB spectra), 5.33 (2H, m, CH$_2$=CH-), 5.92 (1H, m, CH$_2$=CH-), 7.3, 7.45, 7.57, 8.08 (10H, four m, PhCH$_2$OCH$_2$O-, PhCOO-).

Compound 57. A solution of 54 (0.49 g, 1.01 mmol) in MeOH (10 ml) was refluxed with 1 ml 15% NaOH soln. for 1 h. Methanol was removed *in vacuo*, the residue was diluted with water and extracted with $CHCl_3$. The usual extractive isolation gave primary alcohol 55 (0.39 g). This was dissolved in $CH_2Cl_2$ (5 ml) and treated with methanesulfonyl chloride (0.13 ml, 1.2 mmol) in the presence of Et$_3$N (0.335 ml, 2.4 mmol) at -20°C. The reaction mixture was stirred for 1 h at +25°C and quenched with M HCl. Extractive isolation yielded unstable mesylate 56 which was immediately treated with LiBHEt$_3$ (1.5 ml of N soln. in THF) in THF solution (2 ml) at reflux for 1 h. The cooled reaction mixture was successively treated with 15% NaOH soln. (1.5 ml), 30% $H_2O_2$ (1,5 ml) and stirred for 1 h. Then it was diluted with water and extracted with $CHCl_3$. Usual isolation followed by chromatography (hexane-ether 98:2) gave 57 (0.21 g, 56% based on 54), $[\alpha]_D$+80° (C 0.64); $^1$H-NMR: δ 0.08 and 0.1 (6H, two s. *t*BuMe$_2$SiO-), 0.9 (9H, s, *t*BuMe$_2$SiO-), 0.96 (3H, t, Me-14), 1.33 (3H, s, Me-12), 1.33 and 1.68 (2H, two m, H-14, H-14´), 3.5 (1H, dd: 3, 8.5 Hz, H-13), 4.51 and 4.73 (2H, AB-spectrum), 4.72 and 4.86 (2H, AB-spectrum), 5.24 (2H, m, CH$_2$=CH-), 5.9 (1H, m, CH$_2$=CH-), 7.35 (5H, m, PhCH$_2$OCH$_2$O-).

Compound 58. A solution of 57 (0.21 g, 0.57 mmol) were ozonized as it was described for the preparation of compound 27. Pure 58 was obtained by chromatography (hexane-ether 95:5) in 87% yield. $[\alpha]_D^{27}$ +1.7° (C 1.0); $^1$H-NMR (90 MHz): δ 0.12 (6H, s, *t*BuMe$_2$SiO-), 0.9 (9H, s, *t*BuMe$_2$SiO-), 0.99 (3H, t, Me-14), 1.35 (3H, s, Me-12), 1.55 (2H, m, H-14, H-14´), 3.88 (1H, dd, H-13),

4.65 and 4.85 (4H, two AB-spectra), 7.3 (5H, m, PhCH$_2$OCH$_2$O-), 9.6 (1H, s, aldehydic proton).

Compound 59. Compound 51 (0.67 g, 2.3 mmol) was hydrolysed according to the protocol described for the preparation of compound 53. Crude diol 52 (0.46 g, 1.84 mmol) was dissolved in $CH_2Cl_2$ (2 ml) and powdered molecular sieves 3A (an excess), 4-methoxybenzyl methyl ether (0.66 ml, 4.6 mmol), and DDQ (1.04 g, 4.6 mmol) were added under vigorous stirring. Stirring was continued for 30 min at +25°C. The reaction mixture was quenched with sat. $Na_2SO_3$ soln. (5 ml) and filtered through a pad of celite. The filtrate was washed with sat. $NaHCO_3$ soln. Usual extractive isolation followed by chromatography (hexane-EtOAc 4:1) gave 59 (0.53 g, 63% based on 51), $[\alpha]_D^{26}$ +39.7° (C 1.0), $^1$H-NMR: δ 1.5 (3H, s, Me-12), 2.0 (2H, m, H-14, H-14'), 3.82 (3H, s, MeOPhCH<), 4.04 (1H, dd: 8, 5 Hz, H-13), 4.5 (2H, m, H-15, H-15'), 5.29 (2H, m, CH$_2$=CH-), 5.91 (1H, CH$_2$=CH-), 5.92 (1H, s, MeOPhCH<), 6.93 and 8.05 (4H, two m, MeOPhCH<), 7.45 (5H, m, PhCOO-).

Compound 62. A solution of 59 (0.51 g, 1.38 mmol) in MeOH (5 ml) was refluxed for 20 min with 0.5 ml 15% NaOH soln. Methanol was removed *in vacuo* and the residue was diluted with water and exctacted with chloroform. The crude primary alcohol 60 was dissolved in pyridine (3 ml) and $PPh_3$ (0.52 g, 2 mmol) and $CBr_4$ (0.66 g, 2 mmol) were added. The reaction mixture was kept for 1 h at +25°C and quenched with M HCl. Extractive work-up followed by flash chromatography on silica (hexane-EtOAc 9:1) gave 61 (0.36 g, 80%). A solution of 61 in THF (2 ml) was treated with $LiBHEt_3$ (2 ml of 1 N soln. in THF) for 10 min at +25°C. The reaction mixture was quenched by successive addition of 15% NaOH soln. (2 ml) and 30% $H_2O_2$ (2 ml) followed by stirring for 1 h. Extractive isolation followed by chromatography (hexane-EtOAc 9:1) gave 62 (0.52 g, 72% based on 59), $[\alpha]_D^{16}$ -5.8° (C 1.0); $^1$H-NMR: δ 1.07 (3H, t, Me-14), 1.47 (3H, s, Me-12), 1.58 (2H, m, H-14, H-14'), 3.74 (1H, dd: 4.5, 8.5 Hz, H-13), 3.82 (3H, s, MeOPhCH<), 5.25 (2H, m, CH$_2$=CH-), 5.91 (1H, m, CH$_2$=CH-), 5.88 (1H, s, MeOPhCH<), 6.92 and 7.49 (4H, m, MeOPhCH<).

Compound 63. A solution of 62 was ozonized as it was described for the preparation of compound 27. Pure 63 was obtained by chromatography (hexane-EtOAc 4:1) in 89% yield. $[\alpha]_D^{20}$ +32.6° (C 1.0); $^1$H-NMR: δ 1.05 (3H, t, Me-14), 1.4 (3H, s, Me-12), 1.62 (2H, m, H-14, H-14'), 3.82 (3H, s, MeOPhCH<), 3.8 (1H, dd, H-13), 6.0 (1H, s, MeOPhCH<), 6.95 and 7.5 (4H, two m, MeOPhCH<), 9.74 (1H, s, aldehydic proton).

Compound 64. This was prepared by keeping of methylene chloride solution of 62 in the presence of $CF_3COOH$ (traces) for 30 min. Extractive work-up followed by chromatography (hexane-EtOAc 95:5) gave 64 ($R_f$=0.27) and 62

($R_f$=0.24) in 2:1 ratio. $[\alpha]_D^{18}$ +8.5° (C 1.0); $^1$H-NMR: 1.04 (3H, t, Me-14), 1.48 (3H, s, Me-12), 1.55 (2H, m, H-14, H-14′), 3.73 (1H, dd. H-13), 3.82 (3H, s, MeOPhCH<), 5.25 and 5.44 (2H, m, $CH_2$=CH-), 5.94 (1H, m, $CH_2$=CH-), 6.08 (1H, s, MeOPhCH<), 6.9 and 7.45 (4H, MeOPhCH<).

Compound 66. A solution of 65 (0.335 g, 0.93 mmol) in 10:1 THF-water (2.5 ml) was refluxed for 8 hrs in the presence of TsOH·$H_2$O (0.05 g). Acid was neutralysed with $Et_3N$ and the solution was concentrated *in vacuo*. Extractive work-up followed by chromatography (hexane-EtOAc 95:5) gave 66 (0.277 g, 78%), $[\alpha]_D^{28}$ +24° (C 1.0); $^1$H-NMR: δ 1.08 (3H, t, Me-14), 1.42 (3H, s, Me-12), 1.7 (2H, m, H-14, H-14′), 3.65 (1H, m, H-13), 4.43 and 4.62 (2H, AB-spectrum), 4.66 (2H, s, $A^2$-spectrum), 7.35 (10H, m, two $PhCH_2O$-), 9.7 (1H, s, aldehydic proton).

Compound 67. To a solution of 28 (0.023 g, 0.056 mmol) and $Et_3N$ (0.03 ml, 0.266 mmol) in $CH_2Cl_2$ (1 ml) was added tert-butyldimethylsilyl trifluoromethanesulfonate (0.026 ml, 0.113 mmol) at -20°C. The reaction mixture was stirred for 1 h at ambient temperature and quenched with sat. $NaHCO_3$ soln. Extractive isolation followed by chromatography (hexane-ether 99:1) gave 67 (0.029 g, 98%), $[\alpha]_D^{20}$ -9.3° (C 1.5), $^1$H-NMR: δ 0.01 (6H, two s, *t*Bu$Me_2$SiO-), 0.05 (6H, two s, *t*Bu$Me_2$SiO-), 0.88 (9H, s, *t*Bu$Me_2$SiO-), 0.92 (9H, s, *t*Bu$Me_2$SiO-), 0.97 (3H, d: 6.7 Hz, Me-8), 1.02 (3H, d: 7 Hz, Me-4), 1.31 (3H, s, Me-6), 1.47 (1H, dd: 6.2, 15 Hz, H-7), 1.66 (1H, dd: 5 Hz, H-7′), 1.9 (1H, m, H-8), 2.77 (1H, m, H-4), 3.29 (1H, dd: 7.5, 10 Hz, H-9), 3.61 (1H, dd: 5.7 Hz, H-9′), 3.8 (1H, d: 1.5 Hz, H-5), 4.4 and 4.52 (2H, AB-spectrum, $PhCH_2O$-), 4.97 (2H, m, $CH_2$=CH-), 5.93 (1H, m, $CH_2$=CH-), 7.3 (5H, m, $PhCH_2O$-).

Compound 68. A solution of 67 (0.023 g, 0.055 mmol) in 3:6:1 THF-AcOH-$H_2$O (5 ml) was kept for 2 hrs at +50°C and 12 hrs at ambient temperature. Acid was neutralysed with sat. $NaHCO_3$ soln. Extractive work-up followed by chromatography (hexane-EtOAc 87:13) gave 68 (0.014 g, 77%), $[\alpha]_D^{20}$ -12° (C 4.0); $^1$H-NMR: δ 0.1 (6H, d, *t*Bu$Me_2$SiO-), 0.93 (3H, d: 7 Hz, Me-8), 0.95 (9H, s, *t*Bu$Me_2$SiO-), 1.03 (3H, d: 7 Hz, Me-4), 1.4 (3H, s, Me-6), 1.58 (1H, dd: 9, 14.5 Hz, H-7), 1.76 (1H, dd: 3 Hz, H-7′), 1.9 (1H, m, H-8), 2.88 (1H, m, H-4), 3.28 (2H, m, H-9, OH), 3.58 (1H, m, H-9′), 3.87 (1H, d: 1.8 Hz, H-5), 4.41 and 4.5 (2H, m, $CH_2$=CH-), 5.91 (1H, m, $CH_2$=CH-), 7.32 (5H, $PhCH_2O$-).

Compounds 69 and 70. Primary alcohol 68 (0.077 g, 0.18 mmol) was oxidized according to the standard Swern[20] procedure to give the corresponding aldehyde. This was kept in 3% w/w HCl-MeOH (1.5 ml) for 12 hrs at ambient temperature. Acid was neutralyzed with sat. $NaHCO_3$ soln. Extractive work-up followed by chromatography (hexane-ether 93:7) gave 69 (22 mg) and 70 (18 mg). α-Anomer 69: $[\alpha]_D^{20}$ +67.6° (C 0.9); $^1$H-NMR: δ 4.55 (1H, d: 3.2 Hz, H-9), 2.12

(1H, m, H-8), 1.44 (1H, dd: 12.5, 14 Hz, H-$7_{ax}$), 1.85 (1H, dd: 4 Hz, H-$7_{eq}$), 3.47 (1H, d: 4.5 Hz, H-5), 2.77 (1H, m, H-4), 5.93 (1H, m, $CH_2$=C<u>H</u>-), 4.93 and 5.04 (2H, m, $C\underline{H}_2$=CH-), 3.36 (3H, s, -OMe), 0.87 (3H, d: 6.7 Hz, Me-8), 1.2 (3H, d: 6.5 Hz, Me-4), 1.23 (3H, s, Me-6), 4.41 and 4.5 (2H, AB-spectrum, $PhC\underline{H}_2O$-), 7.35 (5H, m, <u>Ph</u>$CH_2O$-).

β-Anomer <u>70</u>: $[\alpha]_D$ -37.8° (C 0.73); $^1$H-NMR: δ 3.93 (1H, d: 8.9 Hz, H-9), 1.9 (1H, m, H-8), 1.07 (1H, dd: 14, 12 Hz, H-7ax), 2.1 (1H, dd: 4 Hz, H-7 eq), 3.15 (1H, d: 4.7 Hz, H-5), 2.82 (1H, m, H-4), 4.91 and 5.03 (2H, m, $C\underline{H}_2$=CH-), 5.91 (1H, m, $CH_2$=C<u>H</u>-), 3.5, s, -OMe), 0.9 (3H, d: 6.5 Hz, Me-8), 1.19 (3H, d: 6.5 Hz, Me-4), 1.21 (3H, s, Me-6), 4.45 (2H, $A^2$-spectrum, $PhC\underline{H}_2O$-), 7.32 (5H, m, <u>Ph</u>$CH_2O$-), nOe: [$H^5$], $H^9$ = 6.2%; [$H^5$], $H^4$ = 13%.

Compounds <u>71</u> and <u>72</u>. These were prepared starting from <u>29</u> according to the procedure described for synthetic sequence <u>28</u> -> <u>69</u> + <u>70</u>.

α-anomer <u>71</u>, $[\alpha]_D^{20}$+58.8° (C 1.0); $^1$H-NMR: δ 4.57 (1H, d: 3.5 Hz, H-9), 2.16 (1H, m, H-8), 1.42 (1H, dd: 13, 14 Hz, H-7ax), 1.85 (1H, dd: 4 Hz. H-7eq), 3.48 (1H, d: 2.5 Hz, H-5), 1.76 (1H, m, H-4), 6.36 (1H, m, $CH_2$=C<u>H</u>-), 4.95 (2H, m, $C\underline{H}_2$=CH-), 3.39 (3H, s, -OMe), 0.86 (3H, d: 7 Hz, Me-8), 1.12 (3H, d: 7 Hz, Me-4), 1.23 (3H, s, Me-6), 4.38 and 4.4 (2H, AB-spectrum, $PhC\underline{H}_2O$-), 7.35 (5H, m, <u>Ph</u>$CH_2O$-).

β-anomer <u>72</u>, $[\alpha]_D^{20}$-43° (C 1.0); $^1$H-NMR: δ 3.92 (1H, d: 8.5 Hz, H-9), 1.91 (1H, m, H-8), 1.05 (1H, dd: 1.5, 12.5 Hz, H-7ax), 2.1 (1H, dd: 4 Hz, H-7eq), 3.12 (1H, d: 3 Hz, H-5), 2.75 (1H, m, H-4), 6.29 (1H, m, $CH_2$=C<u>H</u>-), 4.91 (2H, m, $CH_2$=C<u>H</u>-), 3.5 (3H, s, -OMe), 0.91 (3H, d: 6.7 Hz, Me-8), 1.81 (3H, d: 7 Hz, Me-4), 1.2 (3H, s, Me-6), 4.43 (2H, s, $A^2$-spectrum), 7.35 (5H, m, <u>Ph</u>$CH_2O$-), n.O.e: [$H^5$], $H^9$ = 5%.

Compound <u>73</u>. This was prepared starting from <u>29</u> in 75% yield according to the procedure described for the preparation of compound <u>30</u>. $[\alpha]_D^{20}$ -30.7° (C 1.75); $^1$H-NMR: δ 0.06 (6H, s, *t*Bu<u>Me</u>$_2$SiO-), 0.92 (9H, s, *t*<u>Bu</u>$Me_2$SiO-), 1.02 (3H, d: 6.5 Hz, Me-8), 1.18 (3H, d: 6.7 Hz, Me-4), 1.36 (3H, s, Me-6), 1.46 (1H, dd: 7.5, 1.5 Hz, H-7), 1.75 (1H, dd: 4 Hz, H-7´), 1.87 (1H, m, H-8), 2.67 (1H, m, H-4), 3.37 (1H, dd: 6.5, 10 Hz, H-9), 3.5 (1H, dd: 6 Hz, H-9´), 3.54 (1H, d: 1.8 Hz, H-5), 3.83 (3H, s, <u>Me</u>O$PhCH_2O$-), 4.49 and 4.55 (2H, AB-spectrum), 4.6 and 4.8 (2H, AB-spectrum), 4.98 and 5.03 (2H, m, $C\underline{H}_2$=CH-), 6.1 (1H, $CH_2$=C<u>H</u>-), 6.89 and 7.3 (9H, m, <u>Ph</u>$CH_2O$-, MeO<u>Ph</u>$CH_2O$-).

Compound <u>74</u>. A solution of <u>73</u> (0.365 g, 0.67 mmol) and pyridine (7 ml) in 600 ml $CH_2Cl_2$ was ozonized at -78°C in the presence of Sudan IV (10.5 ml of 0.05% soln.) until discolouration occured. An excess of $Me_2S$ was added and the reaction mixture was slowly warmed to ambient temperature (1.5 h). The solvent was removed *in vacuo*. The residue was evaporated twice with heptane

(20 ml) to remove pyridine,and its solution in $CHCl_3$ passed through a pad of silica. Pure 74 (0.275 g, 75%) was obtained by chromatography (hexane-ether 87:13), $[\alpha]_D^{20}$ -29°; $^1$H-NMR: δ 0.02 (6H, s, *t*BuMe$_2$SiO-), 0.9 (9H, s, *t*BuMe$_2$SiO-), 1.0 (3H, d: 6.5 Hz, Me-8), 1.22 (3H, d: 7 Hz, Me-4), 1.4 (3H, s, Me-6), 1.54 (1H, dd: 14, 6.2 Hz, H-7), 1.81 (1H, dd: 4.5 Hz, H-7´), 1.9 (1H, m, H-8), 2.9 (1H, m, H-4), 3.32 (1H, dd: 9.5, 6.5 Hz, H-9), 3.57 (1H, dd: 5.5 Hz, H-9´), 3.68 (1H, d: 4.5 Hz, H-5), 3.82 (3H, s, MeOPhCH$_2$O-), 4.5 and 4.56 (2H, AB-spectrum), 4.56 and 4.65 (2H, AB-spectrum), 6.89 and 7.3 (9H, m, PhCH$_2$O-, MeOPhCH$_2$O-), 9.85 (1H, d: 2.5 Hz, aldehydic proton).

Compound 76. A solution of 74 (0.026 g, 0.05 mmol) in ether (1 ml) was added to a cooled (-40°C) stirred suspension of $LiAlH_4$ (~0.1 g) in ether (2 ml). Stirring was continued for 20 minutes and then reaction mixture was slowly warmed to ambient temperature and quenched by successive addition of water (0.1 ml), 15% NaOH soln. (0.1 ml), and again water (0.3 ml). The precipitate was separated by filtration. The solvent was evaporated *in vacuo* and the residue was treated with DDQ (0.02 g, 0.075 mmol) in $CH_2Cl_2$ (1 ml) in the presence of powdered 3A molecular sieves (0.1 g) under vigorous stirring. After 20 minutes reaction was quenched with sat. $NaHCO_3$ soln. Extractive work-up followed by chromatography (hexane-ether 88:12) gave 76 (0.023 g, 88%), $[\alpha]_D^{29}$ -21.1° (C 4.4); $^1$H-NMR: δ 0.014 (6H, s, *t*BuMe$_2$SiO-), 0.9 (9H, s, *t*BuMe$_2$SiO-), 0.95 (3H, d: 6.5 Hz, Me-4), 1.0 (3H, d: 6.5 Hz, Me-8), 1.43 (3H, s, Me-6), 1.57 (1H, dd: 14, 5 Hz, H-7), 1.75 (1H, dd: 6.5 Hz, H-7´), 1.97 (1H, m, H-8), 2.2 (1H, m, H-4), 3.3 (1H, dd: 9.5, 7.5 Hz, H-9), 3.5 (1H, dd: 11, 11 Hz, H-3ax), 3.65 (1H, d: 9.5 Hz, H-5), 3.76 (1H, dd: 5 Hz, H-9´), 3.82 (3H, s, MeOPhCH<), 4.06 (1H, dd: 4.5 Hz, H-3), 4.52 and 4.62 (2H, AB-spectrum), 5.46 (1H, s, MeOPhCH<), 6.9 and 7.35 (9H, m, PhCH$_2$O-, MeOPhCH<).

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