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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-GLUCOPYRANOSE (LEVOGLUCOSAN). PART 2.

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Abstract. Stereocontrolled synthesis of erythronolides A and B has been achieved.

In our preceding paper[1] we have described a scheme for the total synthesis of erythronolides A and B (1A and 1B, Scheme 1) the necessary intermediates of which are 3,5-9,11-bis-cyclic derivatives of seco-acids of 9(S)- dihydroerythronolides A and B (2A and 2B). Retrosynthetic transformation of these structures gave C1-C10 segment 4, which is common to both erythronolides, and structurally related aldehydes 3A and 3B which represent C11-C13 segments. Synthesis of these segments from levoglucosan as a common precursor was also described in the preceding publication.

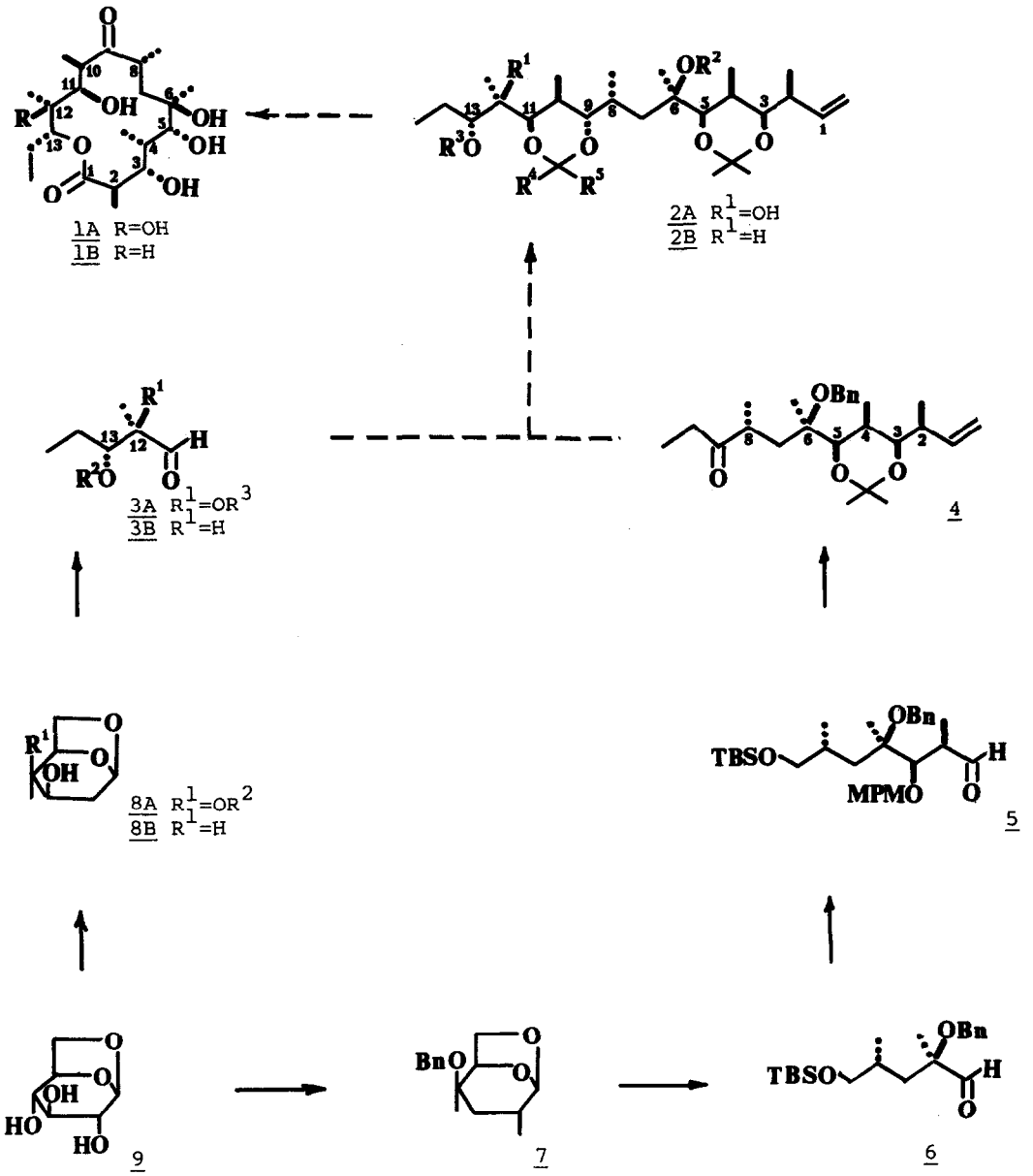
Reported here is the realisation of the key stage of the total synthesis of erythronolides A and B, namely, aldol addition of enolate of the ketone 4 to aldehydes 3A (for erythronolide A), and 3B (for erythronolide B) and transformation of the thus obtained aldols into the target derivatives.

1. Aldol Reaction of Ketone 4 and Aldehydes of Types 3A and 3B

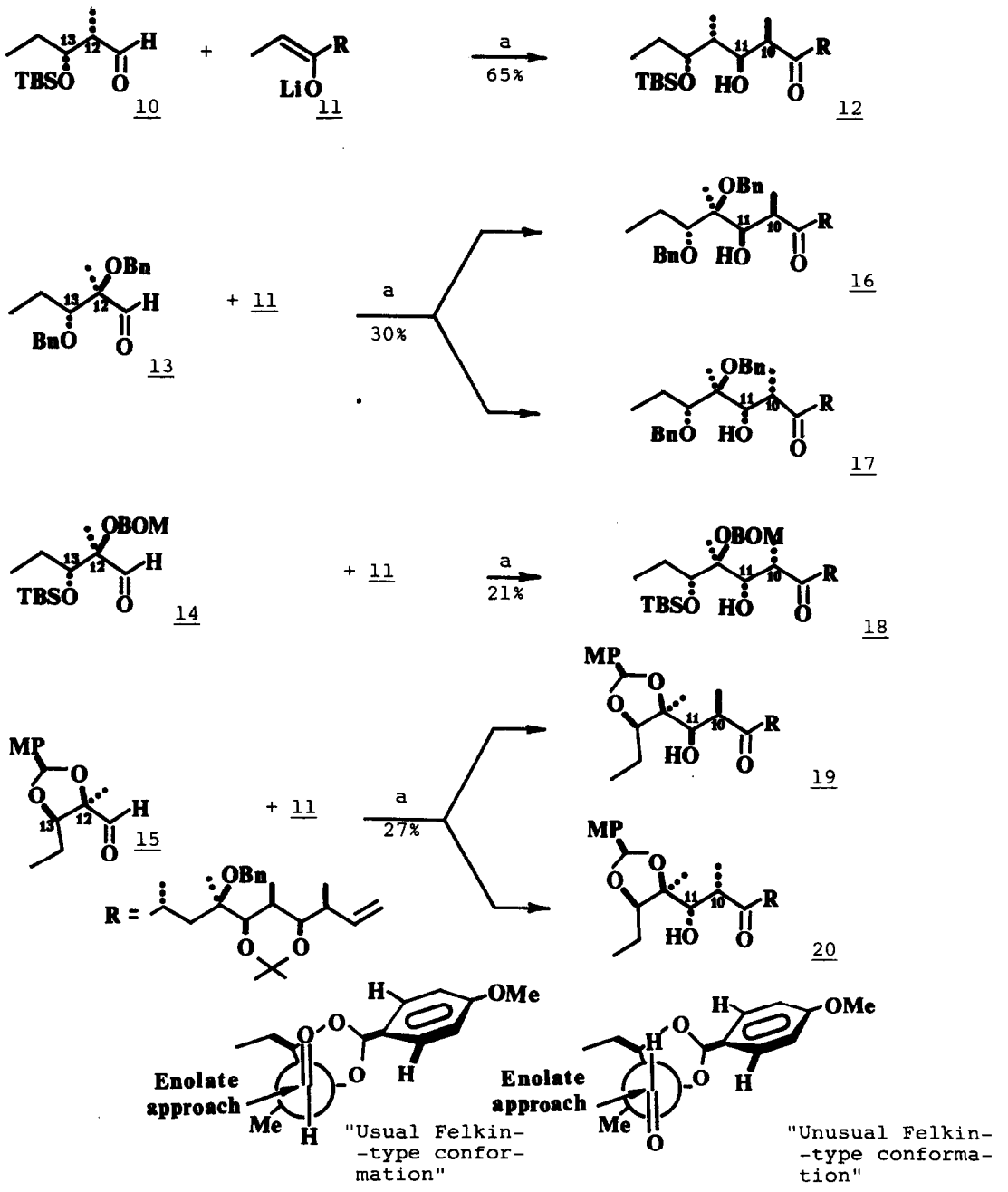
The search of conditions for aldol reaction was based on literature analogies[2,3] which allowed to point to lithium hexamethyldisilazide as an enolising reagent of choice. Addition of Z-(O)-lithium enolate of the ketone 4 (Scheme 2, compound 11) to aldehyde 10 gave, as the only product in 65% yield, hydroxyketone 12 with a correct configuration at C10 and C11 (see below for configurational proof). It is obvious that the aldehyde 10 and enolate 11 represent a matched pair.

More complex pattern was observed in the synthesis of seco-acid of erythronolide A when enolate 11 reacted with dialkoxyaldehydes of the type

Scheme 1


1A R=OH
1B R=H
2A R1=OH
2B R1=H
3A R1=OR3
3B R1=H
4
8A R1=OR2
8B R1=H
TBSO
OBn
MPMO
5
BnO
HO
9
7
6

Scheme 2



a: 4, LiHMDS, -60°/THF, 2 hrs; aldehyde addition at -78°/ 15 min.

3A. Thus, in the case of aldehyde 13 three products were obtained in a total yield of 30%. For two of them, 16 and 17, which form a chromatographically inseparable mixture in a ratio of 4:7 (^{1}H NMR data), was determined *syn*-C10/C11-configuration (it was minor component 16 that possessed the "natural" absolute configuration) and thus the third component is an "*anti*"-isomer. The overall *syn*:*anti* ratio is 3:1. The use of magnesium enolate of the ketone, which is more prone to chelation, did not change the products' ratio.

Addition of the enolate 11 to aldehyde 14 gave also a mixture of three products (4:1:1) in a total yield of 20%, the major isomer possessing "non-natural" 10/11-*syn*-configuration.

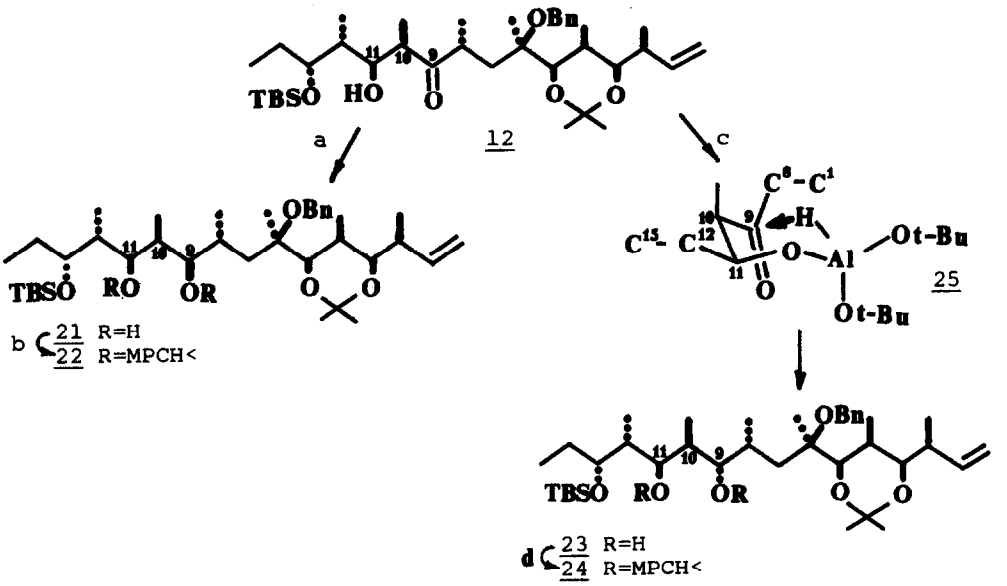
In terms of the double asymmetric induction the addition of the enolate 11 to aldehydes 13 and 14 is a process wherein mismatched pairs of reagents participate and stereochemical outcome of which is determined by direction and magnitude of diastereofacial selection of aldehydes which exceeds the oppositely directed selectivity of the enolate.

According to mechanistic considerations, preferential formation of products with "non-natural" 10/11-*syn*-configuration points to inapplicability of chelate models to the description of stereodirection of addition of lithium enolates to α,β-dialkoxyaldehydes[4]. On the contrary, a prediction of stereochemical outcome of these reactions can correctly be made on the basis of nonchelate Felkin model[5]. In its terms it is possible to rationalise the predominance of a product with the "natural" 10/11-*syn*-configuration upon addition of the enolate 11 to the aldehyde 15. The ratio of the reaction products in this case ("natural"*syn* : "non- natural"*syn* : *anti* = 1.4:1.0:0.4) allows to conclude that reagents form again a mismatched pair. Diastereoselectivity of the reaction, however, is determined by diastereofacial selectivity of the enolate and hence the aldehyde 15 exhibits but small diastereofacial selectivity directed toward "non-natural" configuration at the C11 centre. This may be due to "endo"-orientation of aryl substituent in acetal ring which results in destabilization of the "usual" Felkin-type conformation of aldehyde 15 in favour to the "unusual" one with lesser steric hidrance between aryl substituent and the carbonyl group. These data outline approaches which can be promising in solution of a problem of a control of diastereofacial selectivity of α,β-dialkoxyaldehydes of the type 3A.

2. Synthesis of a Bis-cyclic Precursor of a Seco-acid of 9(S)-Dihydroerythronolide B

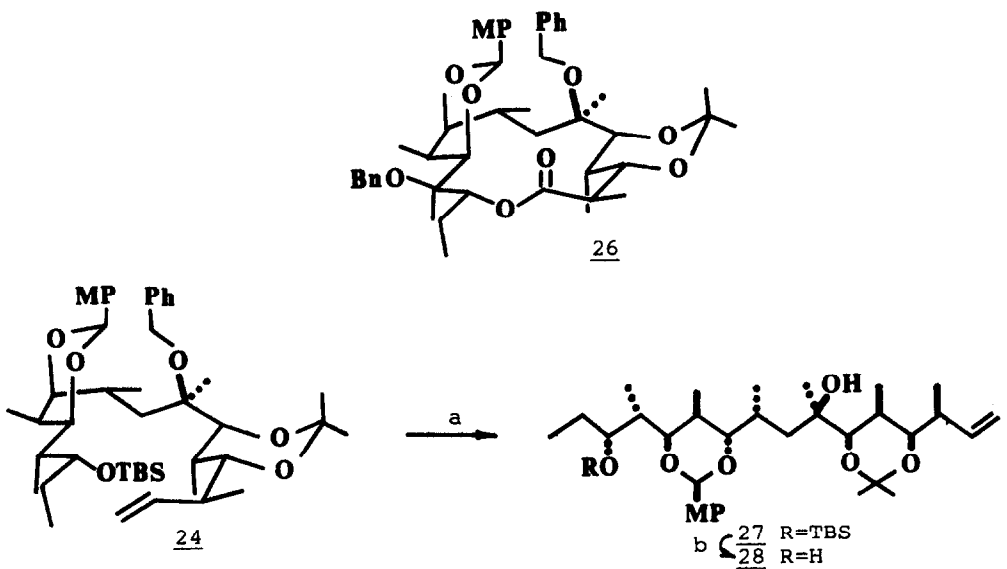
The next steps in the synthesis of the key intermediates, precursors of erythronolides A and B (derivatives 2A and 2B), involved assignment of confi-

Scheme 3



a: $LiBHEt_3/THF$, -78° - -5°, 93%; b: MPMOMe, DDQ, MS 3A/CH_2Cl_2, 23%;
c: $LiAlH(t\text{-}BuO)_3/Et_2O$, -50° - 25°, 86%; d: $MPCH(OMe)_2$, CSA/CH_2Cl_2, 55%.

Scheme 4



a: DDQ/CH_2Cl_2-H_2O, 47%; b: $Bu_4NF.3H_2O/THF$, $+50^{\circ}$, 95%.

guration at the new chiral centres C10 and C11 in the primary products of aldol addition and selective 9/11-*anti* reduction of a keto group therein aimed at establishing the required (S)-configuration at C9.

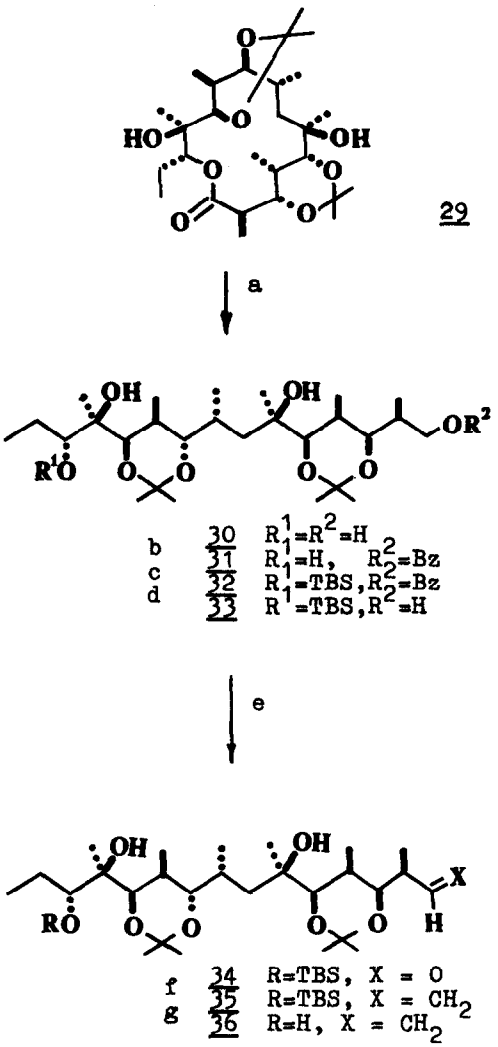
Treatment of hydroxyketone 12 with $LiBHEt_3$ at -78°C gave selectively diol 21, the structure of which was proved following conversion into the cyclic MP-acetal 22 (Scheme 3). Coupling constants ($J_{9,10}$ 1.7, $J_{10,11}$ 2 Hz) indicate relative *syn*-orientation of substituents at C9, C10, and C11 in 22, thus demonstrating C10/C11-*syn* configuration in the starting hydroxyketone 12.

The most suitable agent for "1,3-*anti*" reduction of β-hydroxyketone 12 proved to be $LiAlH(t\text{-}BuO)_3$, selectivity of reduction being 12:1 in favour of diol 23. Coupling constants in the ^{1}H-NMR spectrum of the derived acetal 24 ($J_{9,10}$ 0, $J_{10,11}$ 2.2 Hz) correspond to 9,10-*anti*, 10,11-*syn* orientation of substituents. The observed selectivity seems to be the result of intramolecular attack on the carbonyl group by hydride-ion in a mixed trialkoxyaluminate 25 (cf.[5]).

Compound 28 (Scheme 4) is the required intermediate in the synthesis of erythronolide B and its synthetic utility has already been demonstrated[7]. Transformation of the *anti*-diol 23 into the above intermediate required 6-O-debenzylation, MP-acetalation at 9,11, and deblocking of OH-13. After several trials we took advantage of our observation made in earlier syntheses of erythronolide A derivatives.

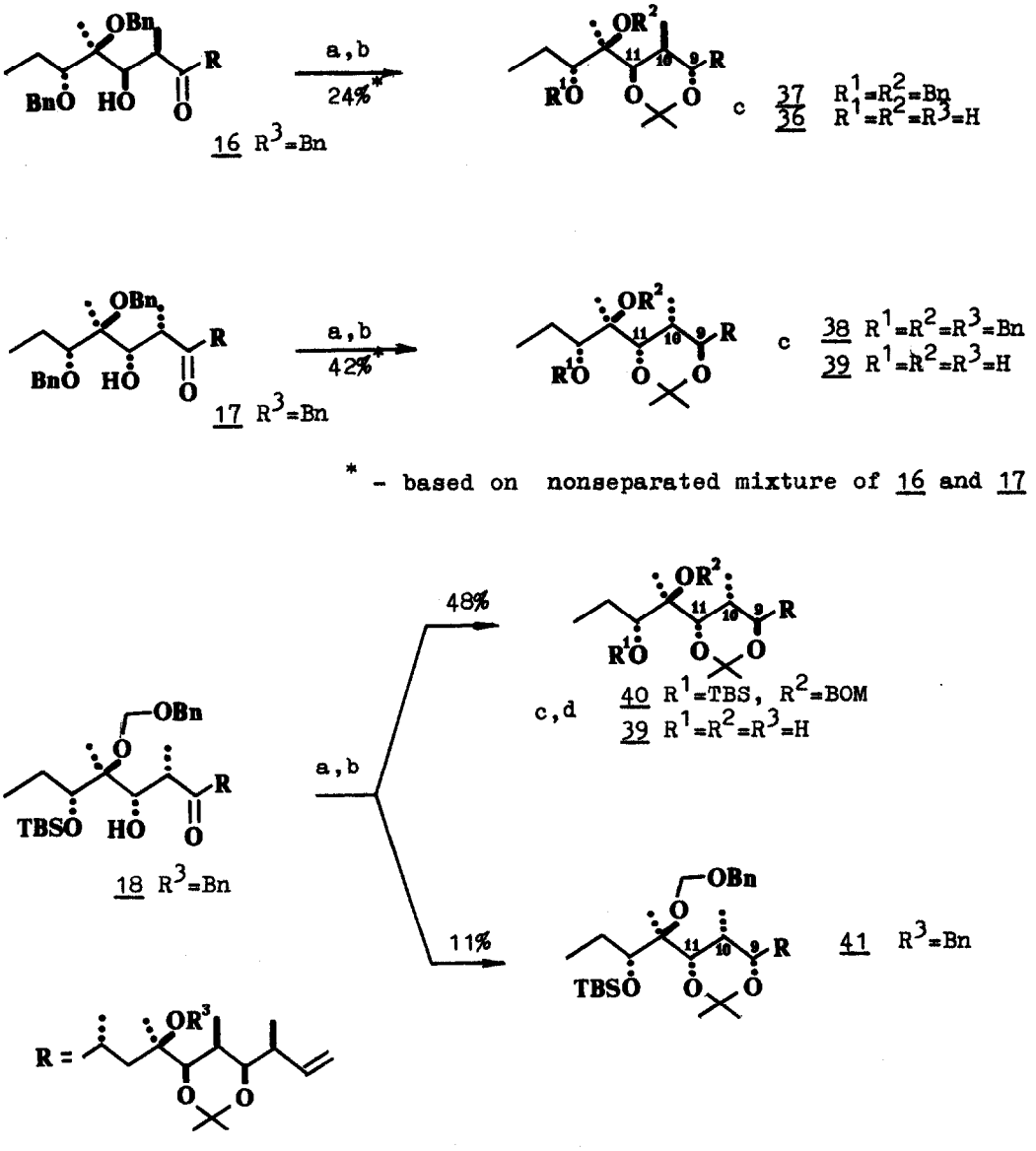
It was found that treatment of 26 (Scheme 4) with DDQ in moist CH_2Cl_2 resulted in rapid 6-O-debenzylation with retention of 9,10-MP acetal and the debenzylation product could be isolated in 50% yield. High rate (cf.[8]) of the process and its unusual chemoselectivity seem to be the consequence of rigid conformation of 26 which results in steric proximity of the axial acetal proton and 6-O-benzyl protective group. Probably, a carbocation formed at the acetal centre upon treatment of 26 with DDQ becomes inaccesible to the water molecule due to steric hindrance of the benzyl group. Thus hydride-ion transfer from the benzyl group onto the carbocation becomes the main process to give a benzylic carbocation which undergoes facile attack by the water to give finally a debenzylation product. In assumption of insignificant difference in conformations of 26 and 24 we anticipated that the latter would undergo analogous debenzylation. This proved to be the case. Compound 24 when treated with DDQ in moist CH_2Cl_2 gave 27 in 47% yield (26% from the diol 23). Desilylation of 27 afforded the target intermediate 28 which proved to be identical to the sample prepared by an independent route[7]. This confirms the correct stereochemistry of all the chiral centres in 23 and, hence, the formation of the "natural" 10/11-*syn* product in aldol addition of the enolate 11 to

Scheme 5



a: $LiAlH_4$/THF, 96%; b: BzCl/Py; c: TBSOTf, Et_3N/CH_2Cl_2; NaOH/MeOH-H_2O, (b,c,d 85%); e: $(COCl)_2$, DMSO, Et_3N/CH_2Cl_2, -60°, 72%; f: PPh_3CH_3Br, n-BuLi/PhH, 88%; g: $Bu_4NF \cdot 3H_2O$, +50°, 95%.

Scheme 6



a: $LiAlH(t\text{-}BuO)_3/Et_2O$; Me_2CO, DMP, CSA; c: Na/NH_3, -78°; d: $Bu_4NF \cdot 3H_2O$, +50°

the aldehyde 10 (Scheme 2).

3. Structural Elucidation of the Primary Aldol Products 16-20.

The structure of products formed upon addition of the enolate 11 to aldehydes of the type 3A was established by direct comparison of derivatives therefrom with the reference compound prepared from the natural erythromycin A. As the reference compound was chosen bis-acetal 36 (Scheme 5) which is also the key intermediate in the synthesis of erythronolide A. Therefore, the transformation sequence of primary aldols 16-20 coincided with the general direction of the synthetic scheme.

The authentic reference sample 36 was prepared from 29 (Scheme 5) which, in turn, was synthesised from erythronolide A according to the known methods[9,10]. Reduction of the lactone 29 with $LiAlH_4$ followed by differential protection of primary and secondary hydroxyls gave 31 which was then conventionally converted into 36.

The structure of compounds 16 and 17 was established following their conversion into derivatives 36 and 39 respectively (Scheme 6) by sequential reduction with $LiAlH(t\text{-}BuO)_3$, acetonation, and debenzylation. The acetonation products, compounds 37 and 38 were isolated in yields of 24 and 42% respectively that clearly points to their origin from the minor and major components in the initial mixture of aldols.

Compound 36 prepared from 37 was identical to the authentic sample. On the basis of practically the same values for coupling constants in ^{1}H-NMR spectra of compounds 37 and 38, the "non-natural 10/11-*syn*" configuration was ascribed to 39.

The reduction-acetalation sequence applied to hydroxyketone 18 gave, besides the major 9,10-*anti*/10,11-*syn* product 40, the minor 9,10-*syn*/ 10,11-*syn* isomer 41 in the ratio of 4:1. Partial deprotection of 40 afforded the aforementioned "non-natural 10/11-*syn*" derivative 39.

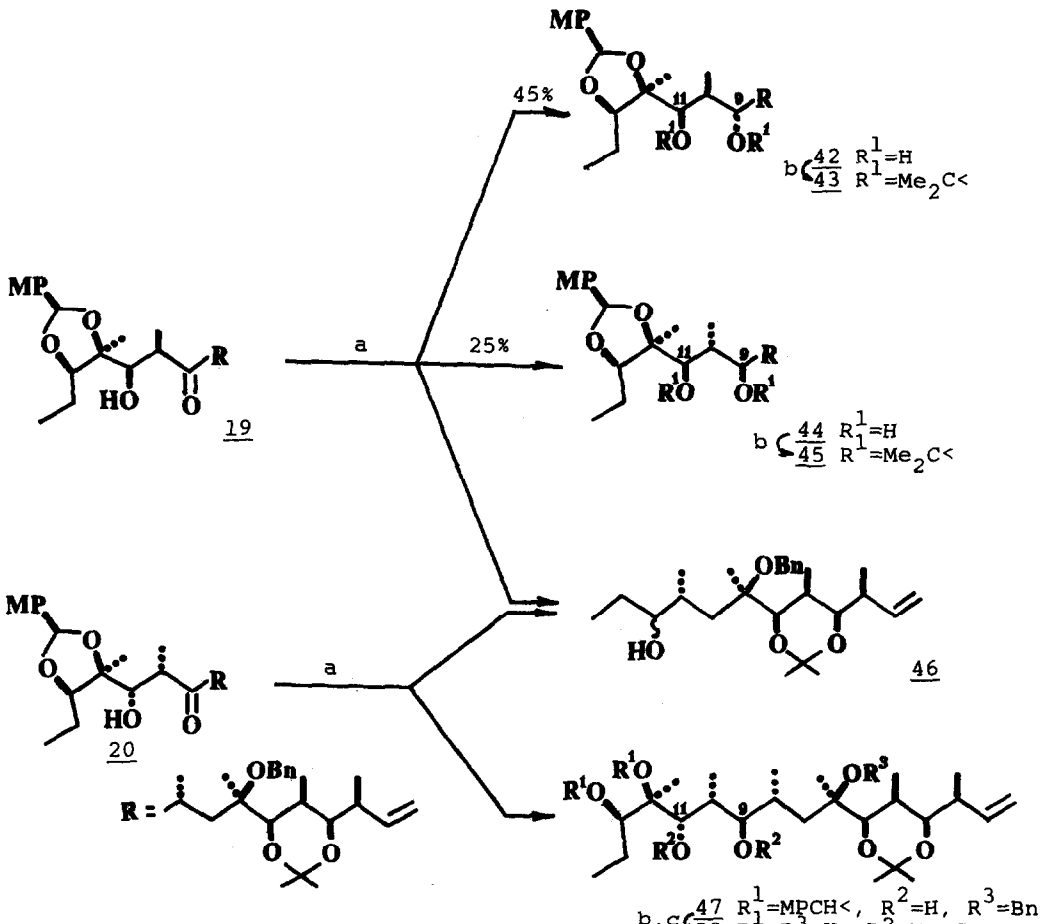
Reduction of hydroxyketone 19 (Scheme 7) led to a mixture of the expected 9,10-*anti*/10,11-*syn* derivative 42 and of approximately the same amount of the 9,10-*anti*/10,11-*anti* isomer 44 together with some secondary alcohols 46. Compounds 42 and 44 were identified following their conversion into cyclic derivatives 43 and 45.

Reduction of hydroxyketone 20 also gave secondary alcohols 46, no 10,11-*anti* product was observed. This could be converted into the aforementioned derivative 39 according to the reaction sequence outlined.

4. Synthesis of 9(S)-Dehydroerythronolide A

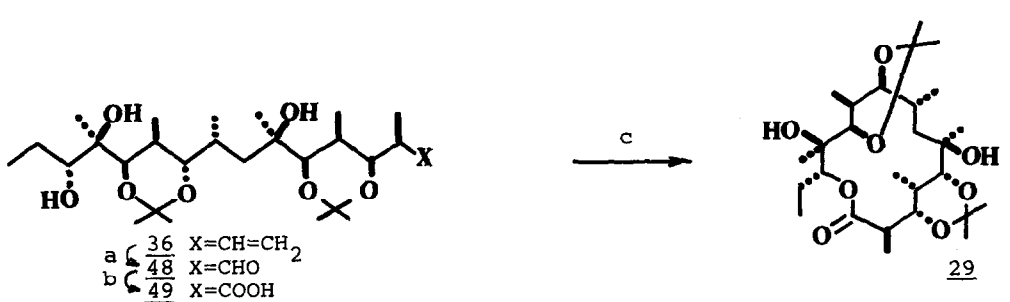
Transformation of the key intermediate into the target product was accomplished as follows. Ozonolysis of the olefin 36 and subsequent oxidation

Scheme 7



a: $LiAlH(t\text{-}BuO)_3/Et_2O$; B: Me_2CO, DMP, CSA; c: Na/NH_3, -78°.

Scheme 8



a: O_3/CH_2Cl_2-1% Py, -78°; b: m-CPBA/THF, pH 7.0 (a,b 70%); c: 2,2-dithiobis(4-t-Bu-1-i-Pr-imidatole), $PPh_3/PhCH_3$, reflux, 20 hrs, $C=10^{-3}M$, 68%.

of the aldehyde formed with *m*-chloroperbenzoic acid gave the hydroxyacid 49 (Scheme 8). This was subjected to macrolactonisation according to a modified Corey procedure[11] to give the lactone 29 in 68% yield. It was completely identical to the sample prepared from the natural erythromycin A. Conversion of 29 into erythronolide A has already been described[12].

EXPERIMENTAL

For general procedures see ref.[1].

Compound 12. To a solution of HMDS (0.247 ml, 1.17 mmol) in THF (4 ml) was added 1.74 N *n*-BuLi/hexane (0.675 ml, 1.17 mmol) at 0°C. After 10 min the reaction vessel was cooled to -60°C and a solution of ketone 4 (0.455 g, 1.06 mmol) in THF (4 ml) was slowly added. After 3 hrs the reaction vessel was cooled to -78°C and a solution of aldehyde 10 (0.276 g, 1.2 mmol) in THF (2 ml) was added dropwise. After additional 15 min the reaction mixture was quenched with sat. NH_4Cl solution at -78°C. The usual extractive work-up followed by chromatography (hexane-ether 88:12) gave 12 (0.44 g, 65%), $[\alpha]_D^{19}$ +13.3° (C 1.95). ^{1}H-NMR: δ 0.07 (6H, s, *t*Bu$\underline{Me}_2$SiO-), 0.57 (3H, d: 6.7 Hz, Me-10), 0.6 (3H, d: 7 Hz, Me-12), 0.87 (9H, s, *t*$\underline{Bu}$$Me_2$SiO-), 0.9 (3H, t, Me-14), 0.91 (3H, d: 7 Hz, Me-4). 1.02 (3H, d: 6.5 Hz, Me-2), 1.13 (3H, d: 7 Hz. Me-8), 1.31 s, 1.37 s (9H, Me- 6, and methyl groups of the isopropylidene moiety), 1.27 (1H, dd: 14.5, 3.3, H-7), 1.49-1.68 (4H, m, H-4, H-12, H-14, H-14'), 2.27 (1H, dd: 9, 14.5 Hz,H-7'), 2.3 (1H, m, H-2), 2.45 (1H, dq: 1.7 Hz, H-10), 3.04 (1H, ddq; H-8), 3.42 (1H, dd: 2, 10 Hz, H-3), 3.75 (1H, m, H-13), 3.92 (1H, d: 2 Hz, H-5), 3.99 (1H, ddd: 10 Hz, H-11), 4.47 and 4.6 (2H, AB-spectrum, Ph$\underline{CH}_2$O-), 5.04 and 5.09 (2H, m, $\underline{CH}_2$=CH-), 5.58 (1H, m, CH_2=$\underline{CH}$-), 7.35 (5H, m, $\underline{Ph}CH_2O$-).

Compounds 16 and 17. Aldol reaction of ketone 4 and aldehyde 13 in the conditions described above for the preparation of compound 12 yielded a mixture of products. Chromatographic separation gave three fractions. The first one contained unchanged ketone 4 (R_f=0.44, hexane-ether 4:1, 0.156 g, 40%). The second fraction contained an individual aldol product (R_f=0.29, 0.05 g, 7%) but the third was again a mixture of two aldols, 16 and 17 (R_f=0.2, 0.157 g, ~23%) in 4:7 ratio (measured on the basis of H-5 integral intensities in ^{1}H-NMR spectra; δ 3.68 and 3.92 p.p.m. for the major and minor constituents respectively).

Compound 18. Aldol reaction of ketone 4 (0.195 g, 0.47 mmol) and aldehyde 14 (0.18 g, 0.49 mmol) in the standard conditions yielded after chromatography (hexane-ether 4:1): unchanged 14 (0.14 g, 0.38 mmol), unchanged 4 (0.124 g, 0.3 mmol), and aldol 18 (0.049 g, 0.062 mmol, R_f=0.32) along with two minor aldols (R_f=0.44, 0.016 g; R_f=0.35, 0.014 g). For 18 $[\alpha]_D^{27}$+14.5° (C

1.0), ^{1}H-NMR: δ 0.05 and 0.06 (6H, two s, *t*BuMe$_2$SiO-), 0.85 (3H, t, Me-14), 0.9 (9H, s, *t*BuMe$_2$SiO-), 0.95, 1.03, 1.13, 1.15 (12H, four d, Me-2, Me-4, Me-8, Me-10), 1.19, 1.22, 1.34, 1.41 (12H, four s, Me-6, Me-12, methyl groups of the isopropylidene moiety), 2.3 (1H, m, H-2), 3.10 (1H, m, H-8), 3.33 (1H, dq: 1.5 Hz, H-10), 3.38 (1H, dd: 2, 10 Hz, H-3), 3.55 (1H, dd, H-13), 3.8 (1H, br.d, H-11), 3.88 (1H, d: 2 Hz, H-5), 4.53 and 4.65 (2H, AB spectrum), 4.61 and 4.62 (2H, AB spectrum), 4.84 and 5.03 (2H, AB spectrum), 5.03 and 5.09 (2H, m, CH$_2$=CH-), 5.57 (1H, m, CH$_2$=CH-), 7.3 (12H, m, PhCH$_2$O-, PhCH$_2$OCH$_2$O-).

Compounds 19 and 20. Aldol reaction of ketone 4 (0.12 g, 0.28 mmol) and aldehyde 15 (0.108 g, 0.43 mmol) in the standard conditions gave after chromatography (hexane-EtOAc 9:1): unchanged 4 (0.087 g, 0.2 mmol), unchanged 15 (0.054 g, 0.2 mmol), and aldols 19 (0.025 g, R_f=0.25, hexane-ether 4:1) and 20 (0.019 g, R_f=0.11) along with a minor aldol (0.008 g, R_f=0.14). 19: $[\alpha]_D^{26}$ +34.9° (C 1.0), ^{1}H-NMR: δ 0.93, 1.01, 1.02, 1.21 (12H, four d, Me-2, Me-4, Me-8, Me-10), 1.05 (3H, t, Me-14), 1.21, 1.3, 1.31, 1.42 (12H, four s, Me-6, Me-12, methyl groups of the isopropylidene moiety), 1.63 (2H, m, H-7, H-14), 1.86 (1H, m, H-14'), 2.3 (1H, m, H-2), 2.35 (1H, dd, H-7), 2.91 (1H, m, H-8), 3.16 (1H, dq: 2.5 Hz, H-10), 3.4 (1H, dd: 2, 10 Hz, H-3), 3.61 (1H, dd: 3.5, 10 Hz, H-13), 3.64 (1H, d, H-11), 3.82 (3H, s, MeOPhCH<), 3.89 (1H, d: 2 Hz, H-5), 4.58 (2H, AB spectrum, PhCH$_2$O-), 5.07 and 5.1 (2H, m, CH$_2$=CH-), 5.7 (1H, m, CH$_2$=CH-), 5.74 (1H, s, MeOPhCH<), 6.9-7.3 (9H, m, PhCH$_2$O-, MeOPhCH<). 20: $[\alpha]_D^{26}$ +32.3° (C 1.0), ^{1}H-NMR: δ 0.89, 1.01, 1.05, 1.11 (12H, four d, Me-2, Me-4, Me-8, Me-10), 0.92 (3H, t, Me-14), 1.15, 1.22, 1.28, 1.36 (12H, four s, Me-6, Me-12, methyl groups of the isopropylidene moiety), 1.6-2.25 (5H, m, H-7, H-7', H-2, H-14, H-14'), 2.89 (1H, m, H-8), 3.15 (1H, dq: 2.5 Hz, H-10), 3.38 (1H, dd: 2, 10 Hz, H-3), 3.73 (1H, d: 2 Hz, H-5), 3.8 (3H, s, MeOPhCH<), 3.9 (1H, d, H-11), 4.42 and 4.55 (2H, AB spectrum, PhCH$_2$O-), 5.03 and 5.09 (2H, CH$_2$=CH-), 5.57 (1H, m, CH$_2$=CH-), 5.68 (1H, s, MeOPhCH<), 6.85, 7.25 (9H, two m, PhCH$_2$O-, MeOPhCH<).

Compound 21. To a solution of 12 (0.028 g, 0.043 mmol) in THF (0.7 ml) was added LiBHEt$_3$ (1 N soln in THF, 0.05 ml) and the reaction mixture was stirred for 1 h at -78°C. Then temperature was raised to -5°C and the reaction was quenched in the usual way (successive addition of 0.01 ml 15% NaOH soln and the equal volume of 30% H_2O_2). Extractive work-up followed by chromatography (hexane-EtOAc 98:2) gave 21 (0.027 g, 93%)m $[\alpha]_D^{28}$+7.6° (C 3.1), ^{1}H-NMR: δ 0.05 and 0.07 (6H, two s, *t*BuMe$_2$SiO-), 0.69 (6H, two d, Me-10, Me-12), 0.8-1.0 (18H, m, *t*BuMe$_2$SiO-, Me-4, Me-8, Me- 14), 1.05 (3H, d: 6.7 Hz, Me-2), 1.25 (1H, dd: 3.5, 14 Hz, H-7), 1.4, 1.45, 1.47 (9H, three s, Me-6,

methyl groups of the isopropylidene moiety), 1.4-1.6 (3H, H-12, H-14, H-14´), 1.64 (2H, m, H-4, H-10), 1.86-2.04 (2H, m, H-7´, H-8), 2.32 (1H, m, H-2), 3.28 (1H, br.d, H-9), 3.45 (1H, dd: 1.6, 10 Hz, H-3), 3.6 (1H, d, H-11), 3.95 (1H, ddd: 5.5, 1.7 Hz, H- 13), 4.03 (1H, d: 2 Hz, H-5), 4.6 and 4.72 (2H, AB spectrum, $PhC\underline{H}_2O$-), 5.04 and 5.1 (2H, m, $C\underline{H}_2$=CH-), 5.58 (1H, m, CH_2=C$\underline{H}$-), 7.3 (5H, m, $\underline{Ph}CH_2O$-).

Compound 23. To a stirred suspension of $LiAlH(t\text{-}BuO)_3$ in ether (prepared from $LiAlH_4$, 0.04 g, 1.05 mmol, and t-BuOH, 0.32 ml, 3.4 mmol) a solution of 12 (0.277 g, 0.428 mmol) in ether (2 ml) was added at -50°C. Cooling was removed and stirring was continued for 1 h. Then the reaction mixture was quenched with solid $Na_2SO_4 \cdot 10H_2O$. After vigorous reaction was completed the reaction mixture was diluted with ether and stirred for additional 1 h. Then inorganics was removed by filtration and the filtrate was concentrated and chromatographed (hexane-ether 88:12) to give 23 (0.24 g, 86%) along with 21 (0.022 g, 7.8%). 23, syrup, $[\alpha]_D^{20}$+22.9° (C 1.85), ^{1}H-NMR: δ 0.1 (6H, s, $t\underline{Bu}Me_2SiO$-), 0.7 (3H, d: 7 Hz, Me-10), 0.77 (3H, d: 6.7 Hz, Me-12), 0.91-0.97 (18 H, m, $t\underline{Bu}Me_2SiO$-, Me-4, Me-8, Me- 14), 1.04 (3H, d: 6.2 Hz, Me-2), 1.36, 1.42, 1.46 (9H, three, s, Me-6, Me-groups of the isopropylidene moiety), 1.5-1.6 (3H, m, H-12, H-14, H- 14´), 1.39 (1H, dd: 5.5, 14 Hz, H-7), 1.68 (1H, dq: 6.5 Hz, H-4), 1.63 (2H, m, H-7´, H-10), 1.98 (1H, m, H-8), 2.33 (1H, m, H-2), 3.43 (1H, dd: 2, 10 Hz, H-3), 3.7 (2H, m, H-13, H-9), 3.9 (1H, d: 2 Hz, H-5), 4.3 (1H, br.d, H-11), 4.6 (2H, s, A^2 spectrum $PhC\underline{H}_2O$-), 5.04 and 5,1 (2H, m, $C\underline{H}_2$=CH-), 5.89 (1H, m, CH_2=C$\underline{H}$-), 7.3 (5H, m, $\underline{Ph}CH_2O$-).

Compound 22. A solution of 21 (0,026 g, 0.04 mmol) and 4- methoxybenzylmethyl ether (0.012 g, 0.08 mmol) in CH_2Cl_2 (1 ml) was treated with DDQ (0.014 g, 0.06 mmol) in the presence of powdered 3A molecular sieves (0.1 g). After 20 min at ambient temperature the reaction was quenched with sat. $NaHCO_3$ soln and molecular sieves removed by filtration. The usual extractive work-up followed by chromatography (hexane- ether 95:5) gave 22 as a sole product (0.007 g, 23%). $[\alpha]_D^{26}$-21.2° (C 1.95), syrup, ^{1}H-NMR: δ 0.05 (6H, s, $t\underline{Bu}Me_2SiO$-), 0.75-0.9 (12H, three d and t, Me-2, Me-4, Me-10, Me-14), 0.9 (9H, s, $t\underline{Bu}Me_2SiO$-), 1.01 (3H. d, Me-8), 1.03 (3H, d, Me-12), 1.15 (1H, dd: 14, 8.7 Hz, H-7), 1.3 (3H, s, Me-6), 1.4, 1.47 (6H, two s, Me-groups of the isopropylidene moiety), 1.4-1.6 (3H, m, H-12, H-14, H-14´), 1.73 (2H, m, H-4, H-10), 2.04 (1H, m, H-2), 2.3 (1H, m, H-8), 2.58 (1H, d, H-7´), 3.3 (1H, dd: 1.7, 10 Hz, H- 9), 3.41 (1H, dd: 2, 10 Hz), H-3), 3.65 (1H, dd: 2, 10 Hz. H-11), 3.79 (3H, s, $\underline{Me}OPhCH<$), 3.86 (1H, d: 2 Hz, H-5), 4.06 (1H, ddd: 1, 6, 6 Hz, H-13). 4.55 and 4.7 (2H, AB spectrum, $PhC\underline{H}_2O$-), 4.95 and 5.05 (2H, $C\underline{H}_2$=CH-), 5.44 (1H, s, $MeOPhC\underline{H}<$), 5.55 (1H, CH_2=C$\underline{H}$-), 6.8, 7.2, 7.36 (9H,

three m, PhCH$_2$O-, MeOPhCH<), nOe [H^9], H$_a$=5%; [H^9], H^{11}=6%.

Compound 24. A solution of 23 (0.095 g, 0.146 mmol) and anisaldehyde dimethyl acetal (0.055 g, 0.33 mmol) in CH_2Cl_2 (2 ml) was kept for 30 min in the presence of catalytic amount of $TsOH \cdot H_2O$. The reaction was quenched with sat. $NaHCO_3$ soln. The usual extractive work-up followed by chromatography (hexane-ether 9:1) gave 24 (0.06 g, 55%), syrup, $[\alpha]_D^{20}$+4.2° (C 3.0). ^{1}H-NMR: δ 0.00 (6H, s, *t*BuMe$_2$SiO-), 0.51 (3H, d: 7 Hz, Me-10), 0.78 (3H, t, Me-14), 0.86 (9H, s, *t*BuMe$_2$SiO-), 1.0 (3H, d: 6, 7 Hz, Me-4), 1.03 (3H, d: 6.5 Hz, Me-2), 1.13 (3H, d: 7 Hz, Me-12), 1.14 (3H, d: 6.5 Hz, Me-8), 1.27 (3H, s, Me-6), 1.35, 1.41 (6H, two s, Me- groups of the isopropylidene moiety), 1.4-1.5 (2H, m, H-14, H-14´), 1.58 (1H, dd, H-7), 1.64 (1H, dd, H-7´´), 1.65 (2H, m, H-4, H-10), 1.89 (1H, m, H-12), 2.33 (1H, m, H-2), 2.43 (1H, m, H-8), 3.31 (1H, d: 10 Hz, H-9), 3.4 (1H, dd: 2, 10 Hz. H-3), 3.62 (3H, s, MeOPhCH<), 3.68 (1H, d: 2Hz, H-5), 3.91 (1H, dd: 2.2, 10 Hz, H-11), 3.99 (1H, ddd: 1.5, 6, 8 Hz, H- 13), 4.66 and 4.77 (2H, AB spectrum, PhCH$_2$O-), 5.05 and 5.11 (2H, CH$_2$=CH-), 5.6 (1H, m, CH$_2$=CH-), 5.56 (1H, s, MeOPhCH<), 6.9, 7.28, 7.43 (9H, three m, PhCH$_2$O-, MeOPhCH<).

Compound 27. To a solution of 24 (0.06 g, 0.078 mmol) in CH_2Cl_2 (1 ml) was added DDQ (0.07 g, 0.3 mmol) in three portions in 1 h at ambient temperature. The reaction was stirred for additional 20 minutes and quenched with sat. $NaHCO_3$ soln. The usual extractive work-up followed by chromatography (hexane-ether 9:1) gave 27 (0.025 g, 47%), $[\alpha]_D^{22}$-3.9° (C 1.25). ^{1}H-NMR: δ 0.05 (6H, s, *t*BuMe$_2$SiO-), 0.73 (3H, d: 7 Hz, Me-10), 0.82 (3H, t, Me-14), 0.91 (9H, s, *t*BuMe$_2$SiO-), 1.0 (3H, d: 6.7 Hz, Me-4), 1.05 (3H, d: 6.5 Hz, Me-2), 1.11 (3H, d: 6.5 Hz, Me-8), 1.18 (3H, d: 7 Hz, Me-12), 1.17 (3H, s, Me-6), 1.43 (6H, s, Me-groups of the isopropylidene moiety), 1.41-1.72 (6H, m, H-14, H-14´, H-7, H-12, H-4), 1.86 (1H, dq, H-10), 2.34 (1H, m, H-2), 2.53 (1H, m, H-8), 3.31 (1H, d: 11 Hz, H- 9), 3.42 (1H, dd: 2, 10 Hz, H-3), 3.5 (1H, d: 2 Hz, H-5), 3.81 (3H, s, MeOPhCH<), 4.02 (1H, ddd: 6.2, 6.2, 1.5 Hz, H-13), 4.05 (1H, dd, 10, 2 Hz, H-11), 5.05 and 5.13 (2H, m, CH$_2$=CH-), 5.61 (1H, m, CH$_2$=CH-), 5.62 (1H, s, MeOPhCH<), 6.9 and 7.45 (4H, two m, MeOPhCH<).

Compound 28. A solution of 27 (0.05 g, 0.06 mmol) and *n*-Bu$_4$NF$\cdot$ 3H$_2$O (0.09 g, 0.3 mmol) in THF (1 ml) was kept at +50°C for 16 hrs. The solution was concentrated *in vacuo*. The residue was dissolved in $CHCl_3$ and washed with brine. The usual work-up followed by chromatography (hexane- EtOAc 3:1) gave 28 (0.032 g, 95%), syrup, $[\alpha]_D^{25}$+6.6° (C 1.0), ^{1}H-NMR: δ 0.78 (3H, d, Me-12), 1.00 (3H, t, Me-14), 1.07 (3H, d, Me-4), 1.05 (3H, d, Me-2), 1.21 (3H, d, Me-10), 1.42 and 1.43 (6H, two s, Me-groups of the isopropylidene moiety), 1.67 (1H, ddq; 2, 2 Hz, H-4), 1.84 (1H, br.dq: 2 Hz, H-10), 1.98 (1H, ddq: 2, 10

Hz, H-12), 2.33 (1H, m: 9.5, 8.2 Hz, H- 2), 2.61 (1H, m: 1.5, 10.5 Hz, H-8), 3.31 (1H, br.d, H-9), 3.42 (1H, dd, H-3), 3.49 (1H, d, H-5), 3.65 (1H, ddd: 5, 7.5 Hz, H-13), 4.17 (1H, dd, H-11), 5.08 (2H, m, $C\underline{H}_2$=CH-), 5.61 (1H, m, CH_2=C$\underline{H}$-), 5.65 (1H, s, MeOPhC$\underline{H}$<), 6.89 and 7.41 (4H, MeO$\underline{Ph}$CH<).

Compound 29. was prepared from natural erythromycin A by the known techniques[9,10]. $[\alpha]_D^{26}$+12.2 (C 1.0), ^{1}H-NMR: δ 0.85 (3H, t, Me-14), 1.01 (3H, d, Me-4), 1.15, 1.23 (6H, two s, Me-6, Me-12), 1.18 (3H, d, Me-2), 1.24 (3H, d, Me-10), 1.28 (3H, d, Me-8), 1.57, 1.58, 1.59 (12H, three s, Me-groups of the isopropylidene moieties), 1.56 (2H, m, H-4, H-14), 1.83 (1H, br.q, H-10), 1.94 (1H, ddd: 2.5, 7.5, 14.5 Hz, H-14'), 2.14 (1H, m, H-8), 2.76 (1H, dq: 6.5, 11 Hz, H-2), 3.13 (1H, d: 11.5 Hz, H-9), 3.6 (1H, d: 1.7 Hz, H-11), 3.79 (1H, dd: 1 Hz, H-3), 3.97 (1H, d: 1.5 Hz, H- 5), 5.06 (1H, dd: 11.5 Hz, H-13).

Compound 30. To a stirred suspension of $LiAlH_4$ (0.412 g, 11 mmol) in ether (5 ml) was added a solution of 29 (0.415 g, 0.829 mmol) in ether (3 ml) at -50°C. Cooling was removed and the reaction mixture was stirred for 1.5 h. Then water (0.412 ml), 15% NaOH soln (0.412 ml), and again water (1.23 ml) were successively added. The precipitate was removed by filtration and the filtrate was concentrated. The residue was chromatographed (hexane-EtOAc 3:7) to give 30 (0.4 g, 95%), glassy solid, $[\alpha]_D^{27}$+35.4° (C 1.0), ^{1}H-NMR: δ 0.97 (3H, d, Me-8), 1.04 (6H, two d, Me-4, Me-2), 1.06 (3H, t, Me-14), 1.1, 1.15, 1.37, 1.4, 1.42 (18 H, five s, Me- 6, Me-12, Me-groups of the isopropylidene moieties), 1.73 (1H, m, H-4), 1.9 (1H, m, H-10), 3.25 (1H, dd: 2, 10 Hz, H-13), 3.34 (1H, dd: 2.5, 6.5 Hz, H-9), 3.49 (1H, d: 2 Hz, H-5), 3.53 (1H, dd: 5, 11 Hz, H-1), 3.62 (1H, dd: 5 Hz, H-1'), 3.62 (1H, dd: 2, 10 Hz, H-3), 3.92 (1H, d: 4 Hz, H-11).

Compound 32. To a solution of 30 (0.4 g, 0.79 mmol) and pyridine (1 ml) in CH_2Cl_2 (2 ml) was added benzoyl chloride (0.185 ml, 1.6 mmol). The reaction mixture was kept for 1 h at ambient temperature and then was quenched with M HCl (20 ml). The usual extractive work-up gave mono- benzoate 31 which was not purified but dissolved in CH_2Cl_2 (2 ml) and treated with tert-butyldimethylsilyl trifluoromethanesulfonate (0.275 ml, 1.2 mmol) for 15 minutes in the presence of Et_3N (0.446 ml, 3.4 ml) at -20°C-->+20°C. The reaction was quenched with M HCl. The usual extractive work-up followed by chromatography (hexane-ether 85:15) gave 32 (0.55 g, 95% based on 30), syrup, $[\alpha]_D^{28}$+21° (C 1.0), ^{1}H-NMR: δ 0.1 (6H, *t*Bu$\underline{Me}_2$SiO-), 0.9 (9H, s, *t*$\underline{Bu}$Me$_2$SiO-), 0.95 (3H, d, Me-8), 1.0 (3H, t, Me- 14), 1.06 (3H, d, Me-4), 1.11 (3H, d, Me-2), 1.11, 1.13, 1.33, 1.42, 1.44 (18H, five s, Me-6, Me-12, Me-groups of the isopropylidene residues), 1.39 (1H, m, H-14), 1.7-1.9 (4H, m, H-8, H-10, H-

14, H-14'), 2.15 (1H, m, H-2), 3.32 (1H, m: 6, 2.5 Hz, H-9), 3.51 (1H, d: 2 Hz, H-5), 3.52 (1H, dd: 1.5, 3.5 Hz, H-13), 3.62 (1H, dd: 2, 10 Hz, H-3), 3.88 (1H, d: 4 Hz, H-11), 4.14 (1H, dd: 11.5, 6.5 Hz, H-1), 4.28 (1H, dd: 5 Hz, H-1'), 7.5 and 8.3 (5H, two m, PhCOO-).

Compound 33. A solution of 32 (0.55 g) in MeOH (10 ml) was refluxed for 40 minutes in the presence of 15% NaOH soln (1 ml). The solvent was removed *in vacuo* and the residue was dissolved in $CHCl_3$ and washed with brine. The usual extractive isolation followed by chromatography gave 33 (0.42 g, 92%), syrup, $[\alpha]_D^{24}$+29.7° (c 1.0). ^{1}H-NMR: δ 0.1 (6H, s, *t*BuMe$_2$SiO-), 0.9 (9H, s, *t*BuMe$_2$SiO-), 0.96 (3H, d, Me-8), 1.00 (3H, t, Me-14), 1.02 (3H, d, Me-2), 1.04 (3H, d, Me-4), 1.07 (3H, d, Me-10), 1.01, 1.16, 1.35, 1.4, 1.42 (18H, five s, Me-6, Me-12, Me-groups of the isopropylidene moieties), 1.76 (1H, m, H-4), 1.8 (2H, m, H-8, H-10), 3.33 (1H, dd: 2.5, 6.7 Hz, H-9), 3.52 (1H, dd: 3.5, 6.5 Hz, H-13), 3.52 (1H, d: 2 Hz, H-5), 3.63 (1H, dd: 2, 10 Hz, H-3), 3.49-3.64 (2H, m, H-1, H- 1'), 3.88 (1H, d: 4 Hz, H-11).

Compound 36. To a stirred suspension of PPh_3CH_3Br (0.68 g, 1.9 mmol) in benzene (5 ml) was added a solution of n-BuLi in hexane (0.9 N, 1.58 ml). The reaction mixture was heated to reflux and a solution of aldehyde 34 in benzene (5 ml) was added dropwise. Refluxing was continued for 10 minutes. Then the reaction mixture was cooled to ambient temperature and several drops of acetone was added. Next, phosphorous contaminants were removed by passing the reaction mixture through a pad of silica (elution with hexane-EtOAc 4:1). The crude 35 was purified by chromatography (hexane-EtOAC 85:15) to give a homogeneous material which however constituted two isomeric products in 4:1 ratio as determined on the basis of integral intensities of the signals of methyl groups in silyl protection, δ 0.1, s; δ 0.17 two s, for major and minor components respectively.

This mixture of isomeric compounds 35 was subjected to desilylation in a usual manner to give after chromatography (hexane-EtOAc 2:1) the only product 36 (0.2 g, 95%), syrup, $[\alpha]_D^{26}$+30.2° (C 1.0), ^{1}H-NMR: δ 0.95- 1.13 (15H, four d and one t, Me-2, Me-4, Me-8, Me-10, Me-14), 1.25, 1.37, 1.39, 1.42 (18H, five s. Me-6, Me-12, methyl groups of the isopropylidene moieties), 1.65 (2H, m, H-4, H-14), 1.9 (3H, m, H-7, H-8, H-10), 2.32 (1H, m, H-2), 3.25 (1H, dd: 2 Hz, H-13), 3.34 (1H, dd: 2.5, 6.5 Hz, H-9), 3.39 (1H, dd: 2, 10 Hz, H-3), 3.45 (1H, d: 2 Hz, H-5), 3.91 (1H, d: 4 Hz, H-11), 5.07 (2H, m, CH_2=CH-), 5.6 (1H, m, CH_2=CH-).

Compounds 37 and 38. To a stirred suspension of $LiAlH(t\text{-}BuO_3)$ (1.2 mmol) in ether (5 ml) a solution of the mixture of compounds 16 and 17 (0.155 g, 0.215 mmol) was added at -50°C. The cooling bath was removed and the reaction

mixture was stirred for 1 h. Then the reaction was quenched in a usual manner (0.046 ml of water, the equal volume of 15% NaOH soln, and 0.14 ml of water) and the precipitate was removed by filtration. The filtrate was concentrated to give crude material (0.17 g). This was dissolved in 1:1 DMP - acetone (2 ml) and kept for 15 minutes at ambient temperature in the presence of catalytic amount of (±)-10- camphorosulfonic acid. The reaction was quenched with sat. $NaHCO_3$ soln. The usual extractive work-up followed by chromatography (hexane-ether 96:4) gave 37 (0.04 g, 24% based on starting mixture 16 and 17) and 38 (0.07 g, 42%).

37: syrup, $[\alpha]_D^{29}$+4.7° (C 1.0), ^{1}H-NMR: δ 0.98 (3H, d, Me-4), 1.0 (3H, d, Me-8), 1.04 (3H, d, Me-10), 1.06 (3H, d, Me-2), 1.14 (3H, t, Me-14), 1.29, 1.31, 1.34, 1.36, 1.43, 1.47 (18H, six s, Me-6, Me-12, Me-groups of the isopropylidene moieties), 1.68 (1H, m, H-4), 1.72 (1H, m, H-14), 1.9 (3H, m, H-8, H-10, H-14'), 2.33 (1H, m, H-2), 3.34, 3.81 (2H, two dd, H- 13, H-9), 3.46 (1H, dd: 2, 10 Hz, H-3), 3.93 (1H, d: 2 Hz, H-5), 4.08 (1H, d: 4.5 Hz, H-11), 4.58 and 4.91 (2H, AB spectrum, PhC$\underline{H}_2$O-), 4.63 and 4.77 (2H, AB spectrum, PhC$\underline{H}_2$O-), 4,64 (2H, A^2-spectra, PhC$\underline{H}_2$O-), 5.08 (2H, m, C$\underline{H}_2$=CH-), 5.6 (1H, CH_2=C$\underline{H}$-), 7.3 (15H, m, 3 x $\underline{Ph}CH_2O$-).

38: syrup, $[\alpha]_D^{28}$-8° (C 1.0); ^{1}H-NMR: δ 0.82 (3H, d, Me-4), 0.97 (3H, t, Me-14), 0.99 (3H, d, Me-10), 1.0 (3H, d, Me-2), 1.07, 1.33, 1.38, 1.39, 1.42 (18H, five s, Me-6, Me-12, Me-groups of the isopropylidene moieties), 1.4 (1H, m, H-4), 1.99 (1H, m, H-8), 2.2-2.3 (2H, m, H-2, H-10), 2.93 (1H, dd: 2, 10 Hz, H-3), 3.08 (1H, dd: 3.5, 8 Hz, H-13), 3.16 (1H, dd: 7.5, 2 Hz, H-9), 3.43 (1H, d: 2 Hz, H-5), 4.06 (1H, d: 4.5 Hz, H-11), 4.47 and 4.56 (2H, AB spectrum, PhC$\underline{H}_2$O-), 4.13 and 4.51 (2H, AB spectrum, PhC$\underline{H}_2$O-), 4.64 and 4.83 (2H, AB spectrum, PhC$\underline{H}_2$O-), 5.12 (2H, m, C$\underline{H}_2$=CH-), 5.6 (1H, CH_2=C$\underline{H}$-), 7.3 (15H, 3 x $\underline{Ph}CH_2O$-).

Compound 36 (synthetic). A solution of 37 (0.04 g) in ether (1ml) was added to an excess of Na/NH_3 (~100 mg Na in ~5 ml NH_3 liq.) at -78°C. The reaction was kept for 1 h at this temperature and then was quenched with solid NH_4Cl until discolouration occured. The reaction mixture was allowed to stand to evaporate NH_3 and then dry residue was diluted with water and extracted with $CHCl_3$. The usual work-up followed by chromatography (hexane-EtOAc 2:1) gave 36 (0.027 g, ~100%), $[\alpha]_D^{27}$+26,4° (C 1.0), ^{1}H-NMR spectrum is identical to that of the authentic sample.

Compound 39. Prepared from 38 according to the procedure described for transformation 37 -> 36 in ~100% yield. Syrup, $[\alpha]_D^{26}$+4.9° (C 1.0), ^{1}H-NMR: δ 0.98, 1.01, 1.03, 1.09 (12H, four d, Me-2, Me-4, Me-8, Me-10), 1.25 (3H, t, Me-14), 1.1, 1.16, 1.32, 1.38-1.39, 1.42 (18H, six s, Me-6, Me-12, Me-groups

of the isopropylidene moieties), 1.65 (1H, m, H-4), 1.78 (1H, m, H-14), 1.8 (1H), 2.05 (2H, m), 3.4 (1H, dd: 2, 10 Hz, H-3), 3.43 (1H, d: 2 Hz, H-5), 3.51 (1H, dd: 2, 10.5 Hz, H-13), 3.78 (1H, d: 3.5 Hz, H-11), 5.06 (2H, $C\underline{H}_2$=CH-), 5.6 (1H, CH_2=$C\underline{H}$-).

Compounds 40 *and* 41. Prepared from 18 (0.05 g) in the standard way: reduction with an excess of LiAlH(*t*-BuO)$_3$ followed by ketalization with DMP-acetone in the presence of catalytic amount of ($\pm$)-10- camphorosulfonic acid. After usual work-up and chromatography (hexane- ether 98:2) compound 40 was obtained in 48% yield along with 41 (11%).

40: syrup, $[\alpha]_D^{28}$+ 21° (C 1.0), ^{1}H-NMR: δ 0.1 (6H, s, *t*Bu$\underline{Me}_2$SiO-), 0.87 (3H, d, Me-10), 0.92 (3H, d, Me-4), 1.01 (3H, t, Me-14), 1.04 (3H, d, Me- 2), 1.09 (3H, d, Me-8), 1.2, 1.28, 1.32, 1.33, 1.43, 1.46 (18H, six s, Me-6, Me-12, Me-groups of the isopropylidene moieties), 1.63 (1H, m, H- 4), 1.9-2.05 (2H, m, H-8, H-14), 2.13 (1H, m, H-10), 2.31 (1H, m, H-2), 3.06 (1H, dd: 3.5, 8 Hz, H-9), 3.43 (1H, dd: 2, 10 Hz, H-3), 3.51 (1H, dd: 4, 6 Hz, H-13), 3.88 (1H, d: 5 Hz, H-11), 3.95 (1H, d: 2 Hz, H-5), 4.48 and 4.6 (2H, AB spectrum), 4.74 and 5.26 (2H, AB spectrum), 5.06 (2H, m, $C\underline{H}_2$=CH-), 5.6 (1H, CH_2=$C\underline{H}$-), 7.3 (10H, m, $\underline{Ph}CH_2O$-, $\underline{Ph}CH_2OCH_2O$-).

41: syrup, $[\alpha]_D^{29}$+26.4° (C 0.33), ^{1}H-NMR: δ 0.1 and 0.15 (6H, two s, *t*Bu$\underline{Me}_2$SiO-), 0.91 (18H, s, *t*$\underline{Bu}Me_2$SiO-), 0.91 (3H, d, Me-10), 0.94 (3H, d, Me-4), 1.03 (3H, d, Me-2), 1.05 (3H, t, Me-14), 1.05 (3H, d, Me-8), 1.3, 1.31, 1.35, 1.36, 1.43, 1.46 (18H, six s, Me-6, Me-12, Me-groups of the isopropylidene moieties), 1.06 (1H, m, H-4), 1.9 (1H, m, H-10), 2.7 (1H, m, H-2), 3.28 (1H, dd: 1.5, 10 Hz, H-9), 3.41 (1H, dd: 2, 10 Hz, H-3), 3.56 (1H, dd: 6, 3.5 Hz, H-13), 3.82 (1H, d: 2 Hz, H-11), 3.91 (1H, d: 2 Hz, H-5), 4.47 and 4.64 (2H, AB spectrum), 4.59 and 4.72 (2H, AB spectrum), 4.75 and 5.18 (2H,m, AB spectrum), 5.05 (2H, m, $C\underline{H}_2$=CH-), 5.55 (1H, m, CH_2=$C\underline{H}$-), 7.3 (10H, m, $\underline{Ph}CH_2O$-, $\underline{Ph}CH_2OCH_2O$-).

Transformation of compound 40 into 39. Compound 40 was debenzylated with Na/NH_3 liq. in the ususal way to give two isomeric compounds: (R_f=0.45 and R_f=0.28, hexane-EtOAc 85:15) in 1:1 ratio. These were desilylated with *n*Bu$_4$NF.3H$_2$0 to give the same compound 39.

Compounds 43, 45, and 46. Compound 19 (9 mg) was reduced with LiAlH(*t*-BuO)$_3$ according to the general procedure. Chromatographic separation of the crude product (hexane-EtOAc 85:15) gave compounds 46 (1 mg, R_f=0.5 hexane-ether 4:1), 42 (4 mg, R_f=0.46), and 44 (2 mg, R_f=0.4). The thus obtained compound 42 (4 mg) was dissolved in acetone-DMP 1:1 (0.5 ml) and kept for 40 min at +20°C in the presence of ($\pm$)-10-camphorosulfonic acid (~1 mg). The reaction mixture was then neutralyzed with excess of Et_3N and concentrated.

Chromatographic purification (hexane-EtOAC 95:5) yielded 43 (3 mg). Syrup, $[\alpha]_D^{25}$-8.8° (C 1.0); ^{1}H-NMR: δ 0.83 (3H, d, Me-10), 0.91 (3H, d, Me-8), 1.03 (3H, d, Me-4), 1.05 (3H, d, Me-2), 1.06 (3H, t, Me-14), 1.24, 1.28, 1.29, 1.35, 1.41 (18H, six s, Me-6, Me-12, Me-groups of the isopropylidene moieties), 1.75 (1H, m, H-8), 1.8 (1H, m, H-4), 2.13 (1H, m, H-10), 2.34 (1H, m, H-2), 3.23 (1H, dd: 3.5, 11 Hz, H-9), 3.42 (1H, dd: 2, 10 Hz, H-3), 3.47 (1H, d: 5.05 Hz, H-11), 3.68 (1H, dd: 10, 4 Hz, H-13), 3.82 (3H, s, MeOPhCH<), 3.84 (1H, d: 2 Hz, H-5), 4.58, 4.73 (2H, AB spectrum, $PhCH_2O$-), 5.07 (2H, m, CH_2=CH-), 5.66 (1H, m, CH_2=CH-), 5.77 (1H, s, MeOPhCH<), 6.9, 7.2-7.5 (9H, m, MeOPhCH<, $PhCH_2O$-).

Compound 45 was prepared starting from 44 by the above described route. Syrup, $[\alpha]_D^{25}$+4.3° (C 0.16); ^{1}H-NMR: δ 0.76 (3H, d, Me-10), 0.94 (3H, d, Me-8), 0.95 (3H, d, Me-4), 0.96 (3H, t, Me-14), 1.04 (3H, d, Me- 2), 1.26, 1.29, 1.31, 1.38, 1.41, 1.45 (18H, six s, Me-6, Me-12, Me- groups of the isopropylidene moieties), 1.64 (1H, m, H-4), 1.75 (1H, m, H-10), 2.10 (1H, m, H-8), 2.32 (1H, m, H-2), 3.44 (1H, dd: 2, 10 Hz, H- 3), 3.48 (1H, dd: 2.5, 10.5 Hz, H-9), 3.59 (1H, d: 10, H-11), 3.68 (1H, dd: 3, 10.5 Hz, H-13), 3.83 (3H, s, MeOPhCH<), 3.89 (1H, d: 2 Hz, H-5), 4.6 (2H, AB spectrum, $PhCH_2O$-), 5.07 (2H, m, CH_2=CH-), 5.68 (1H, m, CH_2=CH-), 5.88 (1H, s, MeOPhCH<), 6.9, 7.2-7.4 (9H, m, $PhCH_2O$-, MeOPhCH<).

For 46 ^{1}H-NMR: δ 0.8-1.1 (12H, Me-2, Me-4, Me-8, Me-9), 2.3 (1H, m, H-2), 3.14 and 3.5 (H-9 of the both isomers), 3.45 (1H, dd, H-3), 4.0 and 3.99 (H-5 of the both isomers), 5.68 (2H, m, CH_2=CH-), 5.78 (1H, m, CH_2=CH-), 7.3 (5H, m, $PhCH_2O$-).

Compound 48. Compound 20 (0.06 g) was reduced with LiAlH(t-BuO)$_3$ according to the described procedure to give after chromatography (hexane - EtOAc 85:15) compound 47 (0.032 g, R_f=0.36 hexane-EtOAc 4:1) along with compound 46 (0.01 g, R_f=0.41). Diol 47 was dissolved in 1:1 acetone-DMP (0.5 ml) and kept for 40 min at+20°C with (±)-10 camphorosulfonic acid (1 mg). The reaction mixture was then neutralyzed with Et_3N and concentrated *in vacuo*. Chromatographic purification (hexane-EtOAc 95:5) yielded 48 (0.029 g, 86%), syrup, $[\alpha]_D^{28}$+4.1° (C 1.0); ^{1}H-NMR: δ 0.99 (3H, d, Me-8), 1.01 (3H, d, Me-10), 1.05 (3H, d, Me-2), 1.08 (3H, d, Me-4), 1.29, 1.3, 1.39, 1.44, 1.47 (18H, five s, Me-12, Me-6; Me-groups of the isopropylidene moieties), 1.77 (1H, m, H-4), 1.92 (1H, m, H-8), 2.02 (1H, m, H-10), 2.33 (1H, H-2), 3.17 (1H, dd: 7, 4.5 Hz, H-9), 3.49 (1H, dd: 2, 10 Hz, H-3), 3.54 (1H, dd: 4.5, 8.5 Hz, H-13), 3.74 (3H, s, MeOPhCH<), 3.89 (1H, d: 2 Hz, H-5), 3.97 (1H, d: 4.5 Hz, H-11), 4.58 and 4.68 d (2H, AB spectrum, $PhCH_2O$-), 5.06 (2H, m, CH_2=CH-, 5.65 (1H, m, CH_2=CH-), 5.76 (1H, s, MeOPhCH<), 6.82, 7.26, 7.4 (9H, m, $PhCH_2O$-, MeOPhCH<).

Compound 29 - synthetic. A solution of compound 36 (0.04 g, 0.075 mmol) in CH_2Cl_2:Py 100:1 (60 ml) was ozonized at-78°C in the presence of Sudan IV dye until discolouration occured. Excess of dimethylsulfide was added and the reaction mixture was slowly warmed to ambient temperature in 1 h. Then the solvent was removed *in vacuo*. The residue was flash chromatographed on silica (hexane-EtOAc 4:1). The thus prepared aldehyde 49 (R_f=0.45, hexane-EtOAc 2:1) was dissolved in THF-phosphate buffer pH 7.0 10:1 (10 ml) and treated with *m*-CPBA (0.05 g). After 30 min at +20°C the reaction mixture was diluted with $CHCl_3$ and washed with $NaHCO_3$. The usual extractive work-up afforded acid 50 (0.029 g, 77%). Unfortunately, compound 50 cannot be purified by usual chromatographic means. Hence crude 50 was directly subjected to lactonization. This was dissolved in toluene (60 ml) and treated with PPh_3 (0.077 g, 0.3 mmol) and 2,2'-dithio- bis(4-tert-butyl-1-*iso*propylimidazole) (0.118 g, 0.3 mmol) for 10 hrs at reflux temperature. Then the half as much amounts of reagents were added and refluxing was continued for additional 10 hrs. Finally, the solvent was removed *in vacuo* and the residue was chromatographed (hexane-EtOAc 4:1) to give 29 (0.019 g, 68%).

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