SYNTHESIS OF MACROLIDE ANTIBIOTICS.

19.† SYNTHESIS OF THE C^7–C^{13} FRAGMENT OF ERYTHRONOLIDE A

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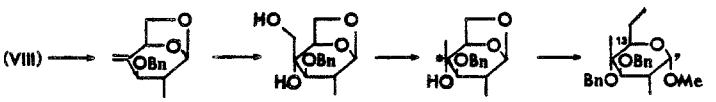
A stereocontrolled synthesis was carried out for the C^7–C^{13} fragment of erythronolide A in 33 steps with an overall yield of 13% relative to starting levoglucosan.

Erythronolides A (I) and B (II) are the major aglycones of a large group of important macrolide antibiotics produced by *Streptomyces erythreus* [2]. Hence, they have become one of the most popular objects for synthetic studies. This is especially true of erythronolide A. We have previously reported the synthesis of erythronolide B from 1,6-anhydro-β-*D*-glucopyranose (levoglucosan). The construction of the carbon skeleton of this product was carried out by two schemes for fusion of fragments: (C^1–C^6) + (C^7–C^{13}) [3, 4] (C^1–C^{10}) + (C^{11}–C^{13}) [1, 5]. Each of these schemes may also be used for the synthesis of erythronolide A. In this and the following communication of this series, we describe the synthesis of erythronolide A (I) by the first fragment fusion scheme. The corresponding retrosynthetic analysis is given in Scheme 1.

As in the case of erythronolide B [3, 4], the key intermediate in the synthesis is the seco-acid of 9-(*S*)-dihydroerythronolide A (III). The cyclic acetal groups in (III) should fix the required conformation of the hydrocarbon chain, which provides for high efficiency of the macrolactonization step. We planned to assemble the hydrocarbon skeleton of seco-acid (III) by the condensation of the C^1–C^6 fragment as ketone (IV), whose synthesis was described in our previous work [3, 6], and the C^7–C^{13} fragment as sulfoxide (V). In turn, sulfoxide (V) may be obtained by the addition of the C^7–C^8 block onto the C^9–C^{13} fragment, namely, aldehyde (VI). The preparation of this aldehyde and its conversion to the C^7–C^{13} fragment of erythronolide A, namely, sulfoxide (V), is the subject of this communication.

In a previous communication, we published the synthesis of the cyclic form of the C^9–C^{13} fragment of erythronolide A, namely, methylglycoside (X) from levoglucosan (VIII) [7]



(IX) (VII) (X)

The construction of the C^{12} site was carried out by epoxidation of methylene derivative (IX) using meta-chloroperbenzoic acid (MCPBA) with subsequent treatment of the mixture of the oxiranes formed by $LiAlH_4$, leading to a 2.7:1 mixture of tertiary alcohols (VII) and its C*-epimer, from which the required isomer (VII) was isolated in overall 56% yield; this isomer was then converted to methylglycoside (X) [7].

†For previous communication, see [1].

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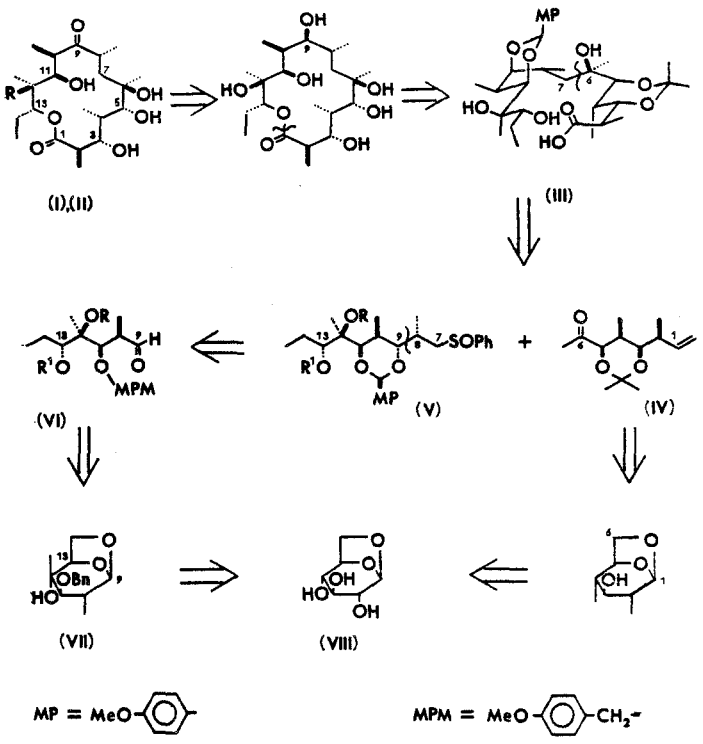
Scheme 1



R = OH (I), H (II).

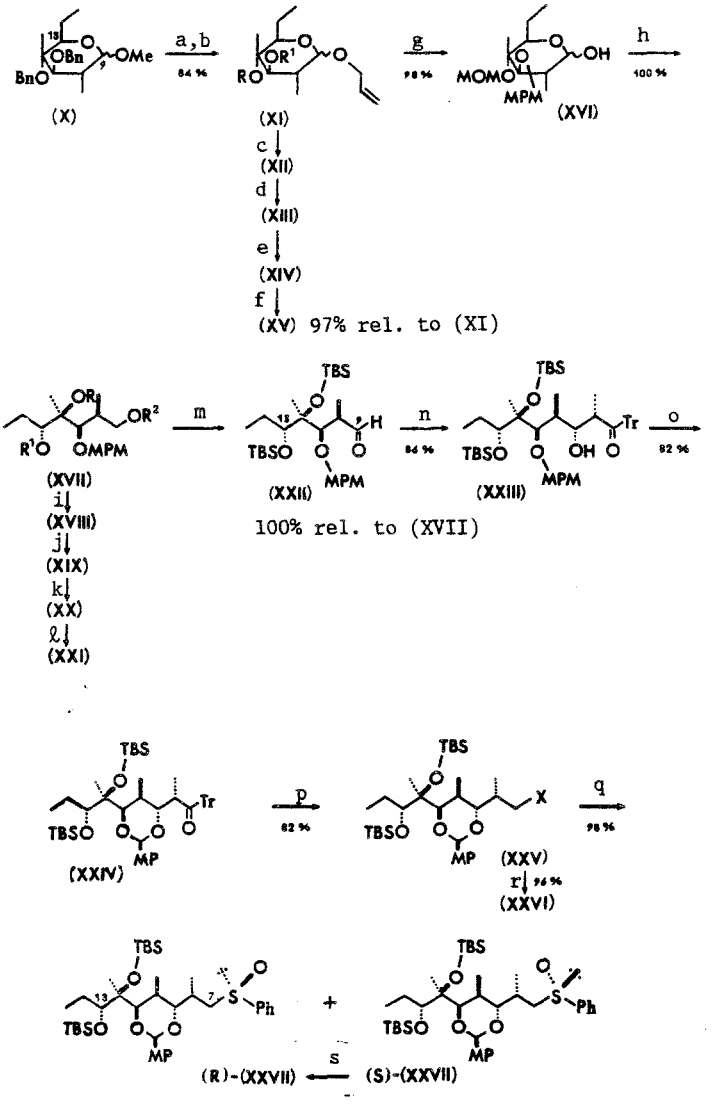
A significant improvement was achieved in the stereoselectivity in constructing the C^{12} site. For this purpose, unsaturated compound (IX) was subjected to catalytic hydroxylation by a system containing 1 mole % OsO_4 and N-methylmorpholine N-oxide (NMMO) [8] with subsequent selective tosylation of the primary hydroxyl group using TsCl/pyridine, closure of the oxirane ring using K_2CO_3 in methanol, and splitting of the oxirane using $LiAlH_4$. The required tertiary alcohol (VII) was obtained as the only product in virtually quantitative yield in four steps. This alcohol was converted by a method described in our previous work [7] into a mixture of isomeric methylglycosides (X), which are cyclic forms of the C^9–C^{13} fragment of erythronolide A. The overall yield of (X) relative to levoglucosan (VIII) was 31.5%.

In accord with the proposed scheme, methylglycosides (X) must be converted to acyclic form and, taking account of the nature of the subsequent transformations, selective protection is required for the hydroxyl groups of this fragment. For this purpose, methylglycosides (X) were debenzylated and the intermediate diols were then converted into a mixture of allyl glycosides (XI) by heating in allyl alcohol at reflux in the presence of catalytic amounts of pyridinium tosylate (PPTS) (see Scheme 2 on the following page). The presence of an O-allylic protective group at C^1 permitted us to effect its selective removal in the presence of protective groups of the other hydroxyl groups, which are labile relative to acidolysis or hydrogenolysis. In order to provide monitoring of the further transformations by spectral and chromatographic methods, the synthetic scheme for the C^7–C^{13} fragment was developed using pure α-allyl glycoside (XI).

The acetylation of (XI) using acetic anhydride in pyridine led to monoacetyl derivative (XII) in quantitative yield. The conversion of (XII) to the methoxymethyl ether (MOM) (XIII) and subsequent deacetylation also proceeded quantitatively and gave (XIV). The fundamentally important *p*-methoxybenzyl (MPM) protection of the hydroxyl group at C^{11} was introduced by the alkylation of (XIV) by *p*-methoxybenzyl chloride (MPMCl). Schemes 1 and 2 show that this group permits a subsequent facile transition from the monoalkyl derivative (XXIII) to acetal (XXIV), which, as discussed above, facilitates the step involving macrolactonization of seco-acid (III).

Selectively protected allyl glycoside (XV) was converted by a reported method [9] to free monosaccharide (XVI). The reduction of (XVI) using $NaBH_4$ in ethanol proceeds rather slowly but gives diol (XVII) in quantitative yield. The yields and absence of side-products

Scheme 2



a — Ra-Ni/EtOH, Δ; b — CH_2=$CHCH_2OH$, PPTS, Δ; c — Ac_2O/Py; d — MOMCl, *i*-Pr_2NEt/CH_2Cl_2; e — MeONa/MeOH; f — NaH, MPMCl/DMF; g — *t*-BuOK/DMSO; $Hg(OAc)_2/Me_2CO—H_2O$; h — $NaBH_4$/EtOH—H_2O; i — BzCl/Py; j — 1MHCl/THF; k — — TBSOTf, Et_3N/CH_2Cl_2, 20°, then TBSOTf, Et_3N/CH_2Cl_2, 100°, ampul; ℓ — NaOH/MeOH—H_2O; m — $(COCl)_2$—DMSO, Et_3N/CH_2Cl_2, —60°; n — $EtCOC(Ph)_3$ — — BuLi/THF; o — DDQ, MS3A/CH_2Cl_2; p — $LiBHEt_3$/THF q — Ph_2S_2—Bu_3P/Py; r — —MCPBA/AcOEt, —40°; s —$(CF_3CO)_2O$, 2, 4, 6-collidine/THF, —78°, then THF —H_2O. R = R^1 = H (XI); R — H, R^1 = Ac (XII); R = MOM, R^1 = Ac (XIII); R = MOM, R^1 = H (XIV); R = MOM, R^1 = MPM (XV); R = MOM, R^1 = R^2 = H (XVII); R = MOM, R^1 = H, R^2 = Bz (XVIII); R = R^1 = H, R^2 = Bz (XIX); R = R^1 = TBS, R^2 = = Bz (XX); R = R^1 = TBS, R^2 = H (XXI); X = OH (XXV); X = SPh (XXVI).

in each step permitted us later to go from (XI) to (XVII), starting from a mixture of anomeric allyl glycosides without separation and complicated chromatographic purification of the intermediates. This is very convenient in the preparation of significant amounts of these compounds.

It was then necessary to convert (XVII) to the C^9–C^{13} fragment of erythronolide A (aldehyde (VI)). In planning the synthesis, we initially intended to use the aldehyde protected at all the hydroxyl groups. For this purpose, tetrol (XVII) was selectively benzoylated at the primary hydroxyl group using 1.1 equivalent of BzCl/pyridine, which, due to the steric hindrance of the hydroxyl group at C^{13}, led exclusively to monobenzoate (XVIII). Then, silylation of the secondary hydroxyl group, removal of the benzoyl group, and oxidation of the intermediate alcohol according to Swern [10] gave a high yield of aldehyde (VI) (R = MOM, R^1 = TBS), which we attempted to use for construction of the carbon chain of seco-acid (III). However, the presence of the MOM protective group at the tertiary hydroxyl group

caused unforeseen difficulties in one of the subsequent steps, such that we had to forego the use of this compound. The use of a silyl protective group for this site proved more successful.

For this purpose, the MOM group was removed by mild acid hydrolysis of benzoate (XVIII) and diol (XIX) was silylated stepwise, starting at the secondary group and, then, under more vigorous conditions, at the tertiary hydroxyl group.* The debenzoylation of bis-TBS ester (XX) gave monohydroxyl derivative (XXI) with overall quantitative yield relative to (XVII). The oxidation of (XXI) according to Swern [10] led to aldehyde (XXII), whose subsequent transformation to the C^7–C^{13} fragment of erythronolide A (sulfoxide (XXVII)) was carried out by our method developed for the synthesis of erythronolide B [3].

The reaction of aldehyde (XXII) with the lithium enolate of ethyl trityl ketone [11] gave 8,9-syn-9,11-anti-aldol (XXIII) as the only product [3, 4]. The treatment of (XXIII) with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) [12] led to cyclic *p*-methoxybenzylidene (MP) acetal (XXIV) as a single isomer relative to the acetal site, whose configuration must later be favorable for the macrolactonization of seco-acid (III) [3]. The reductive cleavage of the tritylcarbonyl group by lithium triethyl borohydride [11] gave primary alcohol (XXV), which, as in a previous case [3, 4], was converted to phenyl sulfide (XXVI). The oxidation of phenyl sulfide ((XXVI) by the action of MCPBA led to a mixture of (*R*)- and (*S*)-sulfoxides (XXVII) in 33 and 65% yield, respectively. The configurations of these products were established on the basis of their specific rotation: $[\alpha]_D$ = +108° for (*R*)-(XXVII) and $[\alpha]_D$ = −19.6° for (*S*)-(XXVII) [13].

During previous studies, we noted that the (*S*)-sulfoxide C^7–C^{13} fragment of erythronolide B, which has a structure similar to (XXVII), has low reactivity relative to C^1–C^6 ketone (IV) [3]. Analogous behavior should have been expected in the case of (*R*)- and (*S*)-sulfoxides (XXVII). Thus, the isomers were separated chromatographically and (*S*)-sulfoxide (XXVII) was isomerized by our method [3] to a mixture of (*R*)- and (*S*)-sulfoxides (XXVII), which were separated in 75 and 22% yield, respectively. This sequence involving the oxidation of sulfide (XXVI), separation, isomerization of the (*S*) isomer, and repeated separation makes (*R*)-sulfoxide (XXVII) a quite available compound.

The product, (*R*)-sulfoxide (XXVII) is a potential C^7–C^{13} fragment of erythronolide A. The use of this derivative in the synthesis of the aglycone of the antibiotic is described in the next article.

EXPERIMENTAL

The melting points were measured on an electrically heated block in a capillary and reported without correction. The specific rotation was measured on a JASCO DIP-360 polarimeter in chloroform (the use of methanol is specifically indicated). The PMR spectra were taken on a Bruker WM-250 spectrometer with $CDCl_3$ as the solvent unless otherwise noted. The signals were assigned by homonuclear double resonance by the difference technique.

The course of these reactions and purity of the isolated compounds were monitored by thin-layer chromatography on plates coated with Kieselgel 60 silica gel. The spots were developed by spraying the plates with 5% sulfuric acid in methanol and subsequent heating to ~200°C.

The reaction mixtures were separated by high-efficiency medium-pressure liquid chromatography on Silpearl silica gel (25-40 μm) in the isocratic mode. A Knauer 88.00 refractometer was used for detection.

The reaction solvents were distilled in an argon atmosphere over a suitable drying agent such as CaH_2 or $LiAlH_4$.

1,6-Anhydro-3-O-benzyl-2-desoxy-2,4-di-C-methyl-β-D-glucopyranose (VII). A sample of 395 mg (1.55 mmole, 1 mole %) OsO_4 was added to a mixture of 35.4 g (143.8 mmoles) olefin (IX) and 42 g (310.6 mmoles, 2.15 eq.) N-methylmorpholine N-oxide in 360 ml 8:1 acetone–water. The mixture was stirred at about 20°C for 40 h, reduced to a volume of 100 ml, diluted with 200 ml chloroform, and washed with 200 ml 10% aq. KOH and water. The aqueous layer was extracted with three 100-ml portions of chloroform. The combined extract was washed with water, 1 *N* hydrochloric acid, and saturated aq. NaCl, dried by filtration through a layer of anhydrous sodium sulfate, and evaporated to dryness. The diol residue (R_f 0.06; the R_f value of starting (IX) in 3:1 benzene–ether was 0.69) was dissolved in 200 ml absolute pyridine. Then, 32.8 g (172.6 mmoles, 1.2 eq.) TsCl was added to the solution. The mixture was maintained at 20°C for 6 h, decomposed by the addition of water, and extracted with chlo-

*An attempt to effect a one-step bis-silylation of diol (XIX) proved unsuccessful.

roform. The extract was washed with 1 *N* hydrochloric acid, water, and saturated aq. NaCl and evaporated to dryness. The residue containing a monotosyl derivative (R_f 0.43 in the same system) was dissolved in 200 ml absolute methanol. Then, 28 g (200 mmoles, 1.4 eq.) K_2CO_3 was added. The mixture was stirred for 15 m in at about 20°C, decomposed with 200 ml water, and extracted with chloroform. The extract was washed with saturated aq. NaCl, dried by filtration through a layer of anhydrous sodium sulfate, and evaporated to dryness. The residue was dissolved in 80 ml abs. ether. To the solution was added slowly with stirring a suspension of 1.9 g (50 mmoles, 1.4 eq.) $LiAlH_4$ in 150 ml abs. ether. The mixture was stirred for 1 h at ~20°C, decomposed by the sequential addition of water, 15% aq. NaOH, and water, and filtered. The precipitate was washed with ether and the solution was evaporated to dryness. The residue consisted of chromatographically and spectrally pure syrupy alcohol (VII). The yield of this product was 38.0 g (100%).

Allyl 2,6-didesoxy-2,4,6-tri-C-methyl-α,β-D-glucopyranoside (XI). A mixture of 9.725 g (25.22 mmoles) (X), 400 ml ethanol, and 160 g Raney nickel was heated at reflux with stirring for 1 h. The catalyst was filtered off and washed with ethanol. The solution was evaporated to dryness. The residue was dissolved in chloroform and purified by filtration through a layer of silica gel and anhydrous sodium sulfate. The diol was eluted with ether. The solution was evaporated to dryness and the residue (4.759 g, 23.299 mmoles) was dissolved in 47.5 ml (698.96 mmoles, 30 eq.) allyl alcohol. Then, 586 mg (10 mole %) PPTS was added and heated at reflux with azeotropic distillation for 5 h (26 ml was distilled off). The mixture was evaporated and the residue was passed through a silica gel layer. The impurities were removed by gradient elution from 9:1 $CHCl_3$–EtOAc to chloroform, while pure (XI) was eluted with 1:1 EtOAc–hexane. The solution was evaporated to dryness. The product yield was 5.08 g (93.9%). A portion of the mixture of (XI) was separated by column chromatography using 3:7 EtOAc–hexane. The α:β anomer ratio was 2:1.

α-(XI), syrup, $[\alpha]_D^{26}$ = +186.4°C (*C* 1.0). PMR spectrum (δ, ppm, *J*, Hz): 1.02 t (3H, CH_3 at C^{14}, $J_{CH_3,14}$ = 7.3), 1.04 d (3H, CH_3 at C^{10}, $J_{CH_3,10}$ = 6.9), 1.14 s (3H, CH_3 at C^{12}), 1.42 m (1H, H^{14}, $J_{14,13}$ = 10, $J_{14,14'}$ = 7.3), 1.73 m (1H, $H^{14'}$, $J_{14',13}$ = 2), 1.79 m (1H, H^{10}, $J_{10,11}$ = 11, $J_{10,9}$ = 3.8), 1.90 and 2.20 br.s (2H, OH at C^{11} and C^{12}), 3.46 d.d (1H, H^{13}), 3.61 d (1H, H^{11}), 3.92 and 4.17 m (2H, $OCH_2CH{=}CH_2$ at C^9), 4.67 d (1H, H^9), 5.18 and 5.30 m (2H, $OCH_2CH{=}CH_2$ at C^9), 5.90 m (1H, $OCH_2CH{=}CH_2$ at C^9).

β-(XI), syrup, $[\alpha]_D^{28}$ = −1.8° (*C* 1.0). PMR spectrum (δ, ppm, *J*, Hz): 1.00 t (3H, CH_3 at C^{14}, $J_{CH_3,14}$ = 7.5), 1.04 d (3H, CH_3 at C^{10}, $J_{CH_3,10}$ = 6.5), 1.15 s (3H, CH_3 at C^{12}), 1.48 m (1H, H^{14}, $J_{14,13}$ = 10.5, $J_{14,14'}$ = 7.5), 1.60 m (1H, H^{10}, $J_{10,9}$ = 9, $J_{10,11}$ = 11), 1.71 m (1H, $H^{14'}$, $J_{14',13}$ = 2), 2.56 and 2.85 br.s (2H, OH at C^{11} and C^{12}), 2.95 d.d (1H, H^{13}), 3.14 d (1H, H^{11}), 4.07 and 4.36 m (2H, $OCH_2CH{=}CH_2$ at C^9), 4.11 d (1H, H^9), 5.19 and 5.28 m (2H, $OCH_2CH{=}CH_2$ at C^9), 5.92 m (1H, $OCH_2CH{=}CH_2$ at C^9).

Allyl 3-O-acetyl-2,6-didesoxy-2,4,6-tri-C-methyl-α-D-glucopyranoside (α-XII). A sample of 1 ml acetic anhydride was added to a solution of 310 mg (1.346 mmoles) α-(XI) in 5 ml pyridine. The mixture was heated for 2 h at 50°C, decomposed by the addition of 1 ml methanol, diluted with water, and extracted with chloroform. The extract was washed with 1 *N* hydrochloric acid, water, and saturated aq. NaCl and dried by filtration through a layer of anhydrous sodium sulfate. The solution was evaporated to dryness and the residue was subjected to chromatography using 2:3 EtOAc–hexane to give 366 mg (100%) (α-XII) as a syrup with $[\alpha]_D^{27}$ = + 200.4° (*C* 1.0). PMR spectrum (δ, ppm, *J*, Hz): 0.94 d (3H, CH_3 at C^{10}, $J_{CH_3,10}$ = 6.0), 1.02 d.t (3H, CH_3 at C^{14}, $J_{CH_3,14}$ = 7.5), 1.12 s (3H, CH_3 at C^{12}), 1.39 m (1H, H^{14}, $J_{14,13}$ = 10.5, $J_{14,14'}$ = 7.5), 1.81 m (1H, $H^{14'}$, $J_{14',13}$ = 2), 1.98 m (1H, H^{10}, $J_{10,9}$ = 3.7, $J_{10,11}$ = 11.6), 2.14 s (3H, $OCOCH_3$ at C^{11}), 2.42 br.s (1H, OH at C^{12}), 3.52 d.d (1H, H^{13}), 3.92 and 4.19 m (2H, $OCH_2CH{=}CH_2$ at C^9), 4.71 d (1H, H^9), 4.93 d (1H, H^{11}), 5.29 and 5.30 m (2H, $OCH_2CH{=}CH_2$ at C^9), 5.89 m (1H, $OCH_2CH{=}CH_2$ at C^9).

Allyl 3-O-acetyl-4-O-methoxymethyl-2,6-didesoxy-2,4,6-tri-C-methyl-α-D-glucopyranoside (α-(XIII)). A sample of 280 μl (3.822 mmoles, 3 eq.) MOMCl was added to a solution of 346 mg (1.274 mmoles) α-(XII) and 665 μl (3.822 mmoles, 3 eq.) *i*-Pr_2NEt in 3 ml methylene chloride. The mixture was heated for 2.5 h at 50°C, diluted with chloroform, washed with 1 *N*

hydrochloric acid, water, and saturated aq. NaCl, dried by filtration through a layer of anhydrous sodium sulfate, and evaporated to dryness. The residue was subjected to chromatography using 3:7 EtOAc–hexane as the eluent to give 394.5 mg (100%) α-(XIII) as a syrup, $[\alpha]_D^{27}$ = +118.8° (*C* 1.0). PMR spectrum (δ, ppm, *J*, Hz): 0.90 d (3H, CH_3 at C^{10}, $J_{CH_3,10}$ = 7.0), 1.01 t (3H, CH_3 at C^{14}, $J_{CH_3,14}$ = 7.5), 1.23 s (3H, CH_3 at C^{12}), 1.36 m (1H, H^{14}, $J_{14,13}$ = 10.5, $J_{14,14'}$ = 7.5), 1.74 m (1H, $H^{14'}$, $J_{14'13}$ = 1.5), 1.93 m (1H, H^{10}, $J_{10,9}$ = 3.5, $J_{10,11}$ = 11), 2.09 s (3H, $OCOCH_3$ at C^{11}), 3.31 s (3H, $OCH_2O\underline{CH_3}$ at C^{12}), 3.65 d.d (1H, H^{13}), 3.92 and 4.18 m (2H, $O\underline{CH_2}CH{=}CH_2$ at C^9), 4.54 and 4.86 d (2H, $O\underline{CH_2}OCH_3$ at C^{12}, AB system, J_{gem} = 8), 4.67 d (1H, H^9), 5.18 and 5.30 m (2H, $OCH_2CH{=}\underline{CH_2}$ at C^9), 5.25 d (1H, H^{11}), 5.89 m (1H, $OCH_2\underline{CH}{=}CH_2$ at C^9).

Allyl 4-O-methoxymethyl-2,6-didesoxy-2,4,6-tri-C-methyl-α-D-glucopyranoside (α-(XIV)). A sample of 0.5 ml 1 *N* MeONa in methanol was added to a solution of 374 mg (1.182 mmoles) α-(XIII) in 5 ml abs. methanol. The mixture was heated for 3 h at 50°C and evaporated to dryness. The residue was dissolved in chloroform, washed with water and saturated aq. NaCl, and dried by filtration through a layer of anhydrous sodium sulfate. The solution was evaporated and the residue was subjected to chromatography using 1:4 EtOAC–hexane to give 324 mg (100%) α-(XIV) as a syrup, $[\alpha]_D^{27}$ = +94.6° (*C* 1.0). PMR spectrum (δ, ppm, *J*, Hz): 1.00 t (3H, CH_3 at C^{14}, $J_{CH_3,14}$ = 7.5), 1.06 d (3H, CH_3 at C^{10}, $J_{CH_3,10}$ = 6.8), 1.15 s (3H, CH_3 at C^{12}), 1.34 m (1H, H^{14}, $J_{14,13}$ = 10.5, $J_{14,14'}$ = 7.5), 1.70 m (1H, $H^{14'}$, $J_{14',13}$ = 2), 1.74 m (1H, H^{10}, $J_{10,11}$ = 11, $J_{10,9}$ = 4), 3.45 s (3H, $OCH_2O\underline{CH_3}$ at C^{12}), 3.50 d.d (1H, H^{13}), 3.60 d.d (1H, H^{11}, $J_{11,OH}$ = 2.5), 3.94 and 4.19 m (2H, $O\underline{CH_2}CH{=}CH_2$ at C^9), 4.32 d (1H, OH at C^{11}), 4.55 and 4.90 d (2H, $O\underline{CH_2}OCH_3$ at C^{12}, AB system, J_{gem} = 8), 4.65 d (1H, H^9), 5.19 and 5.31 m (2H, $OCH_2CH{=}\underline{CH_2}$ at C^9), 5.92 m (1H, $OCH_2\underline{CH}{=}CH_2$ at C^9).

Allyl 3-O-(p-Methoxybenzyl)-4-O-methoxymethyl-2,6-didesoxy2,4,6-tri-C-methyl-α-D-glucopyranoside (α-(XV)). A solution of 322 mg (1.174 mmoles) α-(XIV) in 2 ml DMF was added with stirring to a suspension of 125 mg (5.2 mmoles, 4.44 eq.) NaH in 3.5 ml DMF. After 30 min, 0.318 ml (1.761 mmoles, 1.5 eq.) MPMCl was added. The mixture was stirred for 12 h, decomposed with water, and extracted with ether. The extract was washed with water and saturated aq. NaCl and dried by filtration through a layer of anhydrous sodium sulfate. The solution was evaporated and the residue was subjected to chromatography using 1:4 EtOAc–hexane as the eluent to give 447 mg (96.5%) α-(XV) as a syrup, $[\alpha]_D^{27}$ = +134.0° (*C* 1.0). PMR spectrum (δ, ppm, *J*, Hz): 1.02 t (3H, CH_3 at C^{14}, $J_{CH_3,14}$ = 7.5), 1.05 d (3H, CH_3 at C^{10}, $J_{CH_3,10}$ = 7.0), 1.27 s (3H, CH_3 at C^{12}), 1.38 m (1H, H^{14}, $J_{14,13}$ = 10.5, $J_{14,14'}$ = 7.5), 1.61 m (1H, $H^{14'}$, $J_{14',13}$ = 1.9), 1.87 m (1H, H^{10}, $J_{10,9}$ = 3.5, $J_{10,11}$ = 11), 3.38 s (3H, $OCH_2O\underline{CH_3}$ at C^{12}), 3.54 d.d (1H, H^{13}), 3.58 d (1H, H^{11}), 3.81 s (3H, $OCH_2C_6H_4O\underline{CH_3}$ at C^{11}), 3.92 and 4.19 m (2H, $O\underline{CH_2}CH{=}CH_2$ at C^9), 4.54 and 4.66 d (2H, $O\underline{CH_2}C_6H_4OCH_3$ at C^{11}), AB system, J_{gem} = 11), 4.64 d (1H, H^9), 4.72 and 5.03 d (2H, $O\underline{CH_2}OCH_3$ at C^{12}, AB system, J_{gem} = 7), 5.19 and 5.32 m (2H, $OCH_2CH{=}\underline{CH_2}$ at C^9), 5.92 m (1H, $OCH_2\underline{CH}{=}CH_2$ at C^9), 6.87 and 7.28 m (4H, $OCH_2C_6\underline{H_4}OCH_3$ at C^{11}).

2,6-Didesoxy-3-O-(p-methoxybenzyl)-4-O-methoxymethyl-2,4,6-tri-C-methyl-D-glucopyranose (XVI). A mixture of 447 mg (1.133 mmoles α-(XV) and 160 mg (1.426 mmoles, 1.26 eq.) *t*-BuOK in 2.3 ml DMSO was heated for 2 h at 50°C, diluted with water, and extracted with ether. The extract was evaporated and the residue was dissolved in 5 ml 9:1 acetone–water. Then, 397 mg (1.246 mmoles, 1.1 eq.) $Hg(OAc)_2$ was added. The mixture was maintained for 12 h at about 20°C, evaporated to dryness, diluted with saturated aq. NaCl, and extracted with chloroform. The extract was passed through a layer of silica gel and anhydrous sodium sulfate; (XVI) was eluted with a gradient from 1:9 EtOAc–hexane to 2:3 EtOAc–hexane. The solution was evaporated and the residue was subjected to chromatography using 2:3 EtOAc–hexane as the eluent. The yield of α-(XVI) was 393 mg (98%). The α/β anomer ratio was 1:1 as indicated by PMR spectroscopy (4.68 d (1H, $H^{9-\beta}$, $J_{9,10}$ = 11.0), 5.02 d (1H, $H^{9-\alpha}$, $J_{9,10}$ = 7.5).

Compound (XVII). A sample of 486 mg (12.8 mmoles, 10.3 eq.) $NaBH_4$ was added in 30-mg portions to a solution of 881 mg (2.486 mmoles) (XVI) in 10 ml 9:1 ethanol–water and stirred for 50 h. The mixture was diluted with water, decomposed with acetic acid, poured into water, and extracted with chloroform. The extract was washed with saturated aq. NaCl and

dried by passing through a layer of silica gel and anhydrous sodium sulfate, eluting (XVII) with a gradient from 3:17 EtOAc-benzene to 3:7 EtOAc-benzene.

The solution was evaporated and the residue was subjected to chromatography using ethyl acetate as the eluent to give 886 mg (100%) (XVII) as a syrup, $[\alpha]_D^{25}$ = +9.0° (*C* 1.0). PMR spectrum (δ, ppm, *J*, Hz) (D_2O added): 1.00 t (3H, CH_3 at C^{14}, $J_{CH_3,14}$ = 7.5), 1.02 d (3H, CH_3 at C^{10}, $J_{CH_3,10}$ = 7), 1.29 m (1H, H^{14}), 1.35 s (3H, CH_3 at C^{12}), 1.62 m (1H, $H^{14'}$, $J_{14',13}$ = 2.0, $J_{14,14'}$ = 7.5), 2.20 m (1H, H^{10}, $J_{10,11}$ = 2.4, $J_{10,9}$ = 5.6, $J_{10,9'}$ = 8.5), 3.38 s (3H, $OCH_2O\underline{CH_3}$ at C^{12}), 3.43 d.d (1H, H^9, $J_{9,9'}$ = 11), 3.53 d.d (1H, H^{13}, $J_{13,14'}$ = 10.5), 3.57 d.d (1H, $H^{9'}$), 3.78 s (3H, $OCH_2C_6H_4O\underline{CH_3}$ at C^{11}), 3.79 d (1H, H^{11}), 4.54 d, 4.73 s, 4.58 d (4H, $O\underline{CH_2}OCH_3$ at C^{12} and $O\underline{CH_2}C_6H_4OCH_3$ at C^{11}), 6.85 and 7.23 m (4H, $OCH_2C_6\underline{H_4}OCH_3$ at C^{12}).

Compound (XVIII). A sample of 947 μl (11.70 mmoles, 4 eq.) pyridine and 679 μl (5.85 mmoles, 2 eq.) benzoyl chloride were added to a solution of 1.043 g (2.926 mmoles) (XVII) in 15 ml CH_2Cl_2. The mixture was maintained for 1 h at 20°C, decomposed with water, diluted with chloroform, washed with 1 *N* HCl, water, and saturated aq. NaCl, and dried by filtration through a layer of anhydrous sodium sulfate. The solution was evaporated and the residue was subjected to chromatography using 2:3 EtOAc-hexane as the eluent to give 1.347 g (100%) (XVIII) as a syrup, $[\alpha]_D^{25}$ = +42.6° (*C* 1.0). PMR spectrum (δ, ppm, *J*, Hz) (D_2O added): 1.01 t (3H, CH_3 at C^{14}, $J_{CH_3,14}$ = 7.5), 1.16 d (3H, CH_3 at C^{10}, $J_{CH_3,10}$ = 7), 1.30 m (1H, H^{14}), 1.38 s (3H, CH_3 at C^{12}), 1.62 m (1H, $H^{14'}$, $J_{14',13}$ = 1.7, $J_{11,14'}$ = 7.5), 2.48 d.d.d.q (1H, H^{10}, $J_{10,9}$ = $J_{10,9'}$ = 7, $J_{10,11}$ = 2), 3.38 s (3H, $OCH_2O\underline{CH_3}$ at C^{12}), 3.51 d.d (1H, H^{13}, $J_{13,14}$ = 10.5), 3.73 d (1H, H^{11}), 3.77 s (3H, $OCH_2C_6H_4O\underline{CH_3}$ at C^{11}), 4.23 d (2H, H^9, $H^{9'}$), 4.60 s, 4.68 d, 4.78 d (4H, $O\underline{CH_2}C_6H_4OCH_3$ at C^{11} and $O\underline{CH_2}OCH_3$ at C^{12}), 6.84 and 7.23 m (4H, $OCH_2C_6\underline{H_4}OCH_3$ at C^{11}), 7.45 m, 7.55 m, 8.03 m (5H, $OCOC_6\underline{H_5}$ at C^9).

Compound (XXI). A solution of 1.15 g (2.497 mmoles) (XVIII) in 45 ml 2:1 THF-1 *N* hydrochloric acid was heated for 3 h at 60°C. The mixture was neutralized by the addition of solid sodium bicarbonate, evaporated to dryness, diluted with water, and extracted with chloroform. The extract was dried by filtration through a layer of anhydrous sodium sulfate. The solution was evaporated to dryness and the residue of (XIX) was dissolved in 10 ml CH_2Cl_2. Then, 1.39 ml (10 mmoles, 4 eq.) Et_3N was added and 0.8 ml (3.5 mmoles, 1.4 eq.) TBSOTf was added with cooling to 0°C. The mixture was maintained for 10 min at 20°C, decomposed with saturated aq. $NaHCO_3$, extracted with chloroform, dried by filtration through a layer of anhydrous sodium sulfate, and evaporated to dryness. The residual volatile compounds were removed under vacuum created by an oil pump. The residue was dissolved in 10 ml CH_2Cl_2 and 2.5 ml (17.9 mmoles, 7.1 eq.) Et_3N and 1.6 ml (6.96 mmoles, 2.8 eq.) TBSOTf. The mixture was heated for 17 h at 100°C, decomposed with saturated aq. $NaHCO_3$, extracted with chloroform, washed with 1 *N* hydrochloric acid and saturated aq. NaCl, dried by filtration through a layer of anhydrous sodium sulfate. The solution was evaporated to dryness and the residue of (XX) was dissolved in a mixture of 45 ml methanol and 5 ml 15% aq. NaOH. The mixture was heated at reflux for 1 h. Methanol was evaporated off. The mixture was diluted with water, extracted with chloroform, and dried by passage through a layer of anhydrous sodium sulfate. The solution was evaporated to dryness and the residue was subjected to chromatography using 1:4 EtOAc-hexane to give 1.35 g (100%) (XXI) as a syrup, $[\alpha]_D^{24}$ = +27.5° (*C* 1.0). PMR spectrum (δ, ppm, *J*, Hz): 0.09 and 0.17 s (12H, *t*-Bu($\underline{CH_3}$)$_2$SiO at C^{12} and C^{13}), 0.90 and 0.93 s (18H, *t*-$\underline{Bu}$(CH$_3$)$_2$SiO at C^{12} and C^{13}), 0.97 d (3H, CH_3 at C^{10}, $J_{CH_3,10}$ = 7.0), 0.99 t (3H, CH_3 at C^{14}, $J_{CH_3,14}$ = 7.5), 1.32 s (3H, CH_3 at C^{12}), 1.55 m (1H, H^{14}, $J_{14,13}$ = $J_{14,14'}$ = 7.5), 1.68 m (1H, $H^{14'}$, $J_{14,13}$ = 2.4), 1.88 m (1H, H^{10}, $J_{10,11}$ = 2.4, $J_{9,10}$ = $J_{10,9'}$ = 7.0), 3.44 d (2H, H^9 and $H^{9'}$), 3.55 d.d (1H, H^{13}), 3.57 d (1H, H^{11}), 4.53 and 4.77 d (2H, $O\underline{CH_2}C_6H_4OCH_3$ at C^{11}, AB system, J_{gem} = 11.5), 3.82 s (3H, $OCH_2C_6H_4O\underline{CH_3}$ at C^{11}), 6.88 m and 7.28 m (4H, $OCH_2C_6\underline{H_4}OCH_3$ at C^{11}).

Compound (XXII). A solution of 540 μl (7.6 mmoles, 3.04 eq.) DMSO in 4 ml CH_2Cl_2 was added over 10 min with stirring to a solution of 450 μl (5.065 mmoles, 2.3 eq.) $(COCl)_2$ in 9 ml CH_2Cl_2 at −60°C under argon. The mixture was stirred for 10 min at −60°C and a solution

of 1.35 g (2.497 mmoles) (XXI) in 10 ml CH_2Cl_2 was added over 10 min. The mixture was stirred for 15 min at −60°C and 2.45 ml (17.5 mmoles, 3.5 eq. relative to $(COCl)_2$) Et_3N was added. This mixture was warmed to −5°C, decomposed with 20 ml 1 *N* hydrochloric acid, and extracted with chloroform. The extract was washed with water and saturated aq. NaCl and dried by filtration through a layer of anhydrous sodium sulfate. The solution was evaporated and the residue was subjected to chromatography using 1:24 EtOAc–hexane as the eluent to give 1.34 g (100%) (XXII) as a syrup, $[\alpha]_D^{22} = +8.7°$ (*C* 1.0). PMR spectrum (δ, ppm, *J*, Hz): 0.05 s, 0.07 s, 0.08 s, 0.11 s (12H, *t*-Bu($C\underline{H}_3$)$_2$SiO at C^{12} and C^{13}), 0.86 s and 0.91 s (18H, *t*-$\underline{Bu}$·$(CH_3)_2$SiO at C^{12} and C^{13}), 0.98 t (3H, CH_3 at C^{14}, $J_{CH_3,14} = 7.5$), 1.21 d (3H, CH_3 at C^{10}, $J_{CH_3,10} = 7.8$), 1.25 s (3H, CH_3 at C^{12}), 1.43 m (1H, H^{14}, $J_{14,14'} = J_{13,14} = 7.5$), 1.72 m (1H, $H^{14'}$, $J_{14',13} = 2.3$), 2.77 m (1H, H^{10}, $J_{10,11} = 3.7$, $J_{10,9} = 1.5$), 3.63 d (1H, H^{13}), 3.82 s (3H, $OCH_2C_6H_4OC\underline{H}_3$ at C^{11}), 3.92 d (1H, H^{11}), 4.35 d, 4.42 d (2H, $OC\underline{H}_2C_6H_4OCH_3$ at C^{11}, AB system, $J_{gem} = 11$), 6.85 and 7.22 m (4H, $OCH_2C_6\underline{H}_4OCH_3$ at C^{11}), 9.68 d (1H, H^9).

Compound (XXIII). A sample of 3.6 ml 0.7 *N* *n*-BuLi in hexane (2.55 mmoles, 1.27 eq.) was added to a solution of 797 mg (2.653 mmoles, 1.32 eq.) TrCOEt in 10 ml abs. THF at −78°C. The mixture was stirred for 1 h at −78°C in an argon stream and then a solution of 1.08 g (2.004 mmoles) (XXII) in 8 ml THF was added. The mixture was stirred for 1 h at −78°C, decomposed at −78°C with saturated aq. NH_4Cl, and extracted with chloroform. The extract was washed with saturated aq. NaCl and dried by filtration through a layer of anhydrous sodium sulfate. The solution was evaporated and the residue was subjected to chromatography using 8:92 EtOAc–hexane as the eluent to give 1.449 g (86%) (XXIII) as a syrup, $[\alpha]_D^{25} = +7°$ (*C* 0.8). PMR spectrum (δ, ppm, *J*, Hz): 0.015 s, 0.03 s, 0.12 s (12H, *t*-Bu($C\underline{H}_3$)$_2$SiO at C^{12} and C^{13}), 0.53 d and 0.75 d (6H, CH_3 at C^8 and C^{10}), $J_{CH_3,8} = J_{CH_3,10} = 7$), 0.86 s and 0.91 s (18H, *t*-$\underline{Bu}(CH_3)_2$SiO at C^{12} and C^{13}), 0.95 t (3H, CH_3 at C^{14}, $J_{CH_3,14} = 7.5$), 1.20 s (3H, CH_3 at C^{12}), 1.45 m and 1.58 m (2H, H^{14} and $H^{14'}$), 1.75 m (1H, H^{10}), 2.82 br.d (1H, H^9, $J_{9,10} = 10$), 3.18 br.q (1H, H^8), 3.30 s (1H, OH at C^9), 3.46 d.d (1H, H^{13}, $J_{13,14} = 8$, $J_{13,14'} = 1.9$), 3.81 s (3H, $OCH_2C_6H_4OC\underline{H}_3$ at C^{11}), 3.84 br.s (1H, H^{11}), 4.31 d and 4.58 d (2H, $OC\underline{H}_2C_6H_4OCH_3$ at C^{11}), 6.92 m and 7.25 m (19H, $OCH_2C_6\underline{H}_4OCH_3$ at C^{11} and $(C_6\underline{H}_5)_3CO$ at C^8).

Compound (XXIV). A sample of 3 g powdered 3-Å molecular sieves was added to a solution of 1.449 g (1.726 mmoles) (XXIII) in 15 ml abs. CH_2Cl_2 and, then, a sample of 41 mg (1.812 mmoles, 1.05 eq.) DDQ was introduced. The mixture was stirred for 3 min at 20°C, passed through a layer of Celite, diluted with saturated aq. $NaHCO_3$, and extracted with chloroform. The extract was washed with saturated aq. NaCl, dried by filtration through a layer of anhydrous sodium sulfate, and evaporated. The residue was subjected to chromatography using 8:92 Et_2O–hexane as the eluent to give 1.184 g (82%) (XXIV) as a syrup, $[\alpha]_D^{25} = +4.7°$ (*C* 0.7). PMR spectrum (δ, ppm, *J*, Hz): −0.155 s, −0.08 s, 0.055 s (12H, *t*-Bu($C\underline{H}_3$)$_2$SiO at C^{12} and C^{13}), 0.75 d and 0.96 d (6H, CH_3 at C^8 and C^{10}, $J_{CH_3,10} = J_{CH_3,8} = 6.7$), 0.80 s and 0.91 s (18H, *t*-$\underline{Bu}(CH_3)_2$SiO at C^{12} and C^{13}), 0.93 t (3H, CH_3 at C^{14}, $J_{CH_3,14} = 7.5$), 1.19 s (3H, CH_3 at C^{12}), 3.22 d.d (1H, H^{13}, $J_{13,14} = 2.7$, $J_{13,14'} = 4.5$), 3.58 d (1H, H^{11}, $J_{11,10} = 1.5$), 3.80 s (3H, $=CHC_6H_4OC\underline{H}_3$), 4.07 d (1H, H^9, $J_{9,8} = 9$), 5.23 s (1H, acetal H), 6.86 m, 7.15 m, 7.30 m (19H, $=CHC_6\underline{H}_4OCH_3$ acetal at C^9, C^{11} and $(C_6\underline{H}_5)_3CO$ at C^8).

Compound (XXV). A sample of 20 ml 1 *N* $LiBHEt_3$ in THF (20 mmoles, 1 eq.) was added to 1.184 g (1.415 mmoles) (XXIV) in 10 ml THF. The mixture was maintained for 112 h at 20°C and then decomposed by the consecutive addition with cooling of 18.4 ml 15% aq. NaOH and 18.4 ml 30% aq. H_2O_2. The mixture was stirred for 2 h, diluted with water, and extracted with chloroform. The extract was washed with saturated aq. NaCl and dried by filtration through a layer of anhydrous sodium sulfate. The solution was evaporated to dryness and the residue was subjected to chromatography using 1:3 EtOAc–hexane to give 689 mg (82%) (XXV) as a syrup, $[\alpha]_D^{26} = -20.3°$ (*C* 1.0). PMR spectrum (δ, ppm, *J*, Hz) (added D_2O): −0.075 s, −0.025 s, 0.09 s, 0.10 s (12H, *t*-Bu($C\underline{H}_3$)$_2$SiO at C^{12} and C^{13}), 0.82 s and 0.94 s (18H, *t*-$\underline{Bu}(CH_3)_2$SiO at C^{12} and C^{13}), 0.98 t (3H, CH_3 at C^{14}, $J_{CH_3,14} = 7.5$), 1.11 d and 1.28 d (6H, CH_3 at C^8 and C^{10}, $J_{CH_3,8} = J_{CH_3,10} = 7$), 1.28 s (3H, CH_3 at C^{12}), 1.48-1.72 m (2H, H^{14} and $H^{14'}$), 1.81 m (1H, H^{10}), 2.52 m

(1H, H^8), 3.41 d.d (1H, H^{13}, $J_{13,14} = 10$, $J_{13,14'} = 2.5$), 3.52 d.d (1H, H^9, $J_{9,10} = 1$, $J_{9,8} = 10.5$), 3.62 m (2H, H^7, $H^{7'}$), 3.82 s (3H, $=CHC_6H_4OC\underline{H}_3$), 4.05 d (1H, H^{11}, $J_{10,11} = 2$), 6.66 s (1H, acetal H), 6.90 m, 7.45 m (4H, $=CHC_6\underline{H}_4OCH_3$ acetal at C^9 and C^{11}).

Compound (XXVI). A sample of 363 mg (1.665 mmoles, 2 eq.) Ph_2S_2 and 518 μl (2.08 mmoles, 2.5 eq.) *n*-Bu_3P were added to a solution of 497 mg (0.83 mmole) (XXV) in 5 ml pyridine. The mixture was maintained in an argon atmosphere for 22 h at 20°C, decomposed with water, and extracted with chloroform. The extract was washed with 1 *N* hydrochloric acid, water, and saturated aq. NaCl and dried by filtration through a layer of anhydrous sodium sulfate. The solution was evaporated to dryness and the residue was subjected to chromatography using 1:9 EtOAc–hexane as the eluent to give 550 mg (96%) (XXVI) as a syrup, $[\alpha]_D^{27} = +7.8°$ (*C* 1.0). PMR spectrum (δ, ppm, *J*, Hz): −0.09 s, −0.025 s, 0.08 s, 0.10 s (12H, *t*-Bu($C\underline{H}_3$)$_2$SiO at C^{12} and C^{13}), 0.83 s and 0.94 s (18H, *t*-$\underline{Bu}(CH_3)_2SiO$ at C^{12} and C^{13}), 0.96 t (3H, CH_3 at C^{14}, $J_{CH_3,14} = 7.5$), 1.21 d and 1.25 d (6H, CH_3 at C^8 and C^{10}, $J_{CH_3,8} = J_{CH_3,10} = 7$), 1.42 m (1H, H^{14}, $J_{14,13} = 2$, $J_{14,14'} = 7.5$), 1.60 m (2H, H^{10} and $H^{14'}$), 2.66 m (1H, H^8), 2.76 d.d (1H, H^7, $J_{7,8} = 3.2$, $J_{7,7'} = 12.5$), 3.05 d.d (1H, $H^{7'}$, $J_{7',8} = 3.2$), 3.34 d.d (1H, H^{13}, $J_{13,14'} = 8$), 3.82 s (3H, $=CHC_6H_4OC\underline{H}_3$ acetal at C^9 and C^{11}), 3.49 br.d (1H, H^9, $J_{9,8} = 10$), 3.94 d (1H, H^{11}, $J_{11,10} = 2$), 5.60 s (1H, acetal H), 6.90 m and 7.30 m (9H, $=CHC_6\underline{H}_4OCH_3$ acetal at C^9 and C^{11} and $C_6\underline{H}_5S$ at C^7).

Compound (XXVII). A sample of 5 mg (27.4 μmoles, 1.05 eq.) 85% MCPBA was added to a solution of 18 mg (26.1 μmoles) (XXVI) in 1 ml ethyl acetate at −40°C. The mixture was stirred for 10 min at −40°C, decomposed with saturated aq. $NaHCO_3$, and extracted with chloroform. The extract was washed with saturated aq. NaCl, dried by filtration through a layer of anhydrous sodium sulfate, and evaporated. The residue was subjected to chromatography using 3:7 EtOAc–hexane to give 6 mg (33%) (*R*)-(XXVII) as a syrup, $[\alpha]_D^{28} = +108°$ (*C* 2.0) and 12 mg (65%) (*S*)-(XXVII) as a syrup, $[\alpha]_D^{25} = -19.6°$ (*C* 1.0). PMR spectrum for (*R*)-(XXVII) (δ, ppm, *J*, Hz): −0.07 s, −0.02 s, 0.07 s, 0.09 s (12H, *t*-Bu($C\underline{H}_3$)$_2$SiO at C^{12} and C^{13}), 0.85 s and 0.96 s (18H, *t*-$\underline{Bu}(CH_3)_2SiO$ at C^{12} and C^{13}), 1.02 t (3H, CH_3 at C^{14}, $J_{CH_3,14} = 7.5$), 1.23 d (3H, CH_3 at C^{10}, $J_{CH_3,10} = 7$), 1.28 s (3H, CH_3 at C^{12}), 1.37 d (3H, CH_3 at C^8, $J_{CH_3,8} = 6.5$), 1.52-1.80 m (3H, H^{10}, H^{14}, $H^{14'}$), 2.34 d.d (1H, H^7, $J_{7,8} = 11$, $J_{7,7'} = 13$), 2.71 d.d (1H, $H^{7'}$, $J_{7',8} = 2$), 3.05 m (1H, H^8), 3.32 d.d (1H, H^{13}, $J_{13,14} = 8$, $J_{13,14'} = 2$), 3.33 br.d (1H, H^9, $J_{9,8} = 10$), 3.82 s (3H, $=CHC_6H_4OC\underline{H}_3$ acetal at C^9, C^{11}), 4.07 d (1H, H^{11}, $J_{11,10} = 2$), 5.68 s (1H, acetal H), 6.90 m and 7.43 m (4H, $=CHC_6\underline{H}_4OCH_3$ acetal at C^9, C^{11}), 7.52 m and 7.63 m (5H, $SOC_6\underline{H}_5$ at C^7).

PMR spectrum for (*S*)-(XXVII) (δ, ppm, *J*, Hz): −0.11 s, −0.02 s, 0.08 s, 0.10 s (12H, *t*-Bu($C\underline{H}_3$)$_2$SiO at C^{12} and C^{13}), 0.815 s and 0.93 s (18H, *t*-$\underline{Bu}(CH_3)_2SiO$ at C^{12} and C^{13}), 0.98 t (3H, CH_3 at C^{14}, $J_{CH_3,14} = 7.5$), 1.22 d (3H, CH_3 at C^{10}, $J_{CH_3,10} = 7$), 1.27 s (3H, CH_3 at C^{12}), 1.29 d (3H, CH_3 at C^8, $J_{CH_3,8} = 6$), 1.54 m (2H, H^{14}, $H^{14'}$), 1.64 m (1H, H^{10}), 2.62 m (2H, H^7, H^8), 2.81 d.d (1H, $H^{7'}$, $J_{7,7'} = 13.5$, $J_{7',8} = 9$), 3.33 d.d (1H, H^{13}, $J_{13,14} = 2$, $J_{13,14'} = 8$), 3.48 d.d (1H, H^9, $J_{9,10} = 2$, $J_{9,8} = 8.5$), 3.79 d (1H, H^{11}, $J_{11,10} = 2.5$), 3.82 s (3H, $=CHC_6H_4OC\underline{H}_3$ acetal at C^9, C^{11}), 5.59 s (1H, acetal H), 6.90 m and 7.42 m (4H, $=CHC_6\underline{H}_4OCH_3$ acetal at C^9, C^{11}), 7.55 m (5H, $SOC_6\underline{H}_5$ at C^7).

Isomerization of (S)-(XXVII) to (R)-(XXVII). A sample of 8 μl (61.2 μmoles, 3.6 eq.) 2,4,6-collidine was added to a solution of 12 mg (17 μmoles) (*S*)-(XXVII) in 0.5 ml THF cooled to −60°C and then a solution of 2.9 μl (20.4 μmoles, 1.2 eq.) TFAA in 200 μl THF was introduced with stirring in an argon atmosphere. The mixture was stirred for 20 min at −60°C. Then, 500 μl 4:1 THF–H_2O was added and the mixture was warmed to 20°C, diluted with chloroform, washed with 1 *N* hydrochloric acid, water, and saturated aq. NaCl, dried by filtration through a layer of anhydrous sodium sulfate, and evaporated to dryness. The residue was subjected to chromatography using 3:7 EtOAc–hexane as the eluent. The yield of (*R*)-(XXVII) was 9 mg (75%), while the yield of (*S*)-(XXVII) was 2.6 mg (21.7%).

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