CONCLUSIONS

1. A rearrangement was discovered of 1,6-anhydro-2-desoxy-2,4-di-C-methyl-3-O-benzyl-4-O-mesyl-β-D-glactopyranose into 1,6-anhydro-2-desoxy-2,4-di-C-methyl-3-O-benzyl-5-O-mesyl-α-L-idofuranose.

2. The C^{13}-epi-C^9–C^{13} fragment of erythronolide A was synthesized from levoglucosan in 18 stages in an overall yield of 3.4%.

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SYNTHESIS OF MACROLIDE ANTIBIOTICS. COMMUNICATION 7.*

NEW SYNTHESIS OF C^9–C^{13} FRAGMENT OF ERYTHRONOLIDE A

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In the preceding article [1], we described the synthesis of the 13-epi-C^9–C^{13} fragment of erythronolide A, based on the isomerization of the mesylate of tertiary alcohol (I). In this reaction, a 4-methylene derivative (II) is formed as a side product [1, 2], which was previously used to prepare the C^9–C^{13} fragments of erythronolide B and oleandonolide [3]. In the present work, we carried out a new synthesis of this important intermediate product and also improved the synthesis of the C^9–C^{13} fragment of erythronolide A (see following page).

We used levoglucosan (III) as the starting material from which the oxide (IV) was obtained in four stages [4]. In contrast to the case of 4-O-benzyl analog (V), the yield of oxide (IV) is 10 higher, and, what is most important, it can readily be purified by vacuum distillation, so that the chromatography of large amounts of the material can be avoided.

The reaction of oxirane (IV) with Me_2Mg in ether [5] gives the alcohol (VI) in a practically quantitative yield. In the PMR spectrum of this compound, there is a signal of a methyl group (δ, ppm 1.14 d, J_{2,CH_3} = 7.5 Hz) and of a hydroxyl group (2.72, br. d), and the highest SSCC $J_{1,2} = J_{2,3} = 1$ Hz are similar to those observed in the 4-O-benzyl analogy [5], and correspond to the diaxial position of the substitutents at C^2 and C^3. Because of the presence at O^4 of a readily and selectively removable protecting group, a large variety of protecting groups can be introduced into alcohol (VI) O^3, the most suitable being the O-benzyl group. The benzylation of alcohol (VI) proceeds to give a high yield of the protected product. The subsequent removal of the allyl protection by a known method [6] and oxidation of alcohol (VIII) obtained in the DMSO–$(COCl)_2$ system according to [7] leads to the intermediate ketone (IX). The PMR and ^{13}C NMR spectra of this ketone are similar to the spectrum of the 3-O-methyl derivative [5]. The position of the proton signals and their multiplicity indicate the retention of the 1,6-anhydropyranose system.

*For Communication see [7].

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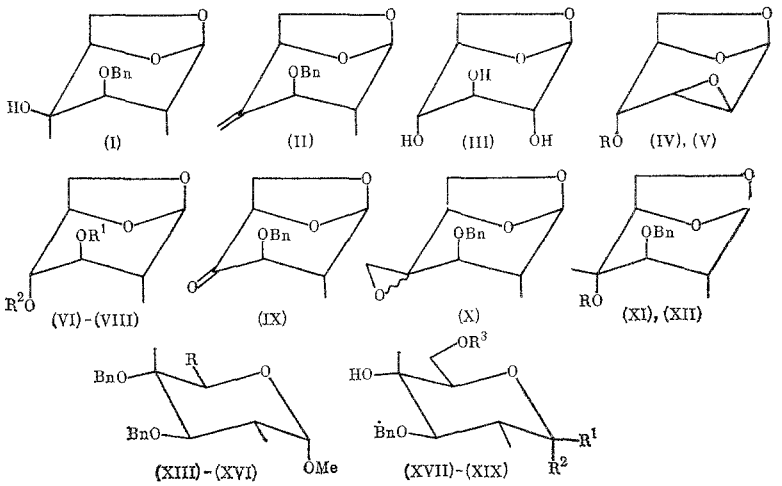

R = $CH_2CH=CH_2$ (IV); R = Bn (V); R^1 = H, R^2 = $CH_2CH=CH_2$ (VI); R^1 = Bn, R^2 = = $CH_2CH=CH_2$ (VII); R^1 = Bn, R^2 = H (VIII); R = H (XI); R = Bn (XII); R = CH_2OH (XIII); R = CHO (XIV); R = $-CH=CH_2$ (XV); R = CH_2CH_3 (XVI); R^1 = R^3 = H, R^2 = = OMe (XVII); R^2 = R^3 = H, R^1 = OMe (XVIII); R^1 = H, R^2 = OMe, R^3 = Ms (XIX).

The reaction of ketone (IX) with $Ph_3P=CH_2$ in benzene leads to the derivative (II) already described in [2]. In its epoxidation by m-chloroperbenzoic acid in $CHCl_3$, a mixture of oxiranes (X) is formed, which, without separation, was reduced by $LiAlH_4$ in THF, and then chromatographed on silica gel. Two tertiary alcohols were thus obtained, one of which corresponds to the D-galactomer (I) (23%) already described in [8], and the other to the glucoderivative (XI) (56%). The last compound has a stereochemistry corresponding to that of the C^9–C^{13} fragment of erythronolide A. To complete the synthesis, the propagation of the carbon chain at C^6 has only to be effected.

Initially an attempt was made to conclude the synthesis of this fragment by the reaction of 6-O-mesyl derivative (XIX) with organocopper compounds, similar to that already described in [2] for the corresponding galacto derivative. Alcohol (XI) was methanol used, and the mixture of α- (XVII) and β-methylglycosides (XVIII) was separated. The spectral data of the compounds obtained confirm that assumed structure: (XVII) — $J_{1,2}$ = 3.5 $J_{2,3}$ = 10, (XVIII) — $J_{1,2}$ = 8.5, $J_{2,3}$ = 10.8 Hz. The α-anomer (XVII) was selectively transformed into mesylate (XIX) and introduced into the reaction with M_2CuLi. However, instead of the expected replacement of the mesyloxy group by a methyl group, demesylation took place. Such a sharp difference between the mesylates (XIX) isomeric at C^4 and the corresponding D-galacto isomer [2] can probably be explained by the participation in the substitution reaction of the hydroxyl group at C^4.

Since the C^9–C^{13} fragment of erythronolide A could not be obtained via the α-anomer (XVII), a method of chain propagation at C^6 was used, which had already been employed in the synthesis of other fragments [3]. Dibenzyl ether (XII), whose structure was confirmed not only by PMR and ^{13}C NMR spectra, but also by x-ray diffraction analysis,* was methanolyzed, and the mixture of α- and β-anomers (XIII) formed was separated by chromatography. The PMR spectra of these compounds were used to reliably determine the configuration of the anomeric center and confirm their structure (α-(XIII) $J_{1,2}$ = 3.5, $J_{2,3}$ = 11 Hz; β-(XII) $J_{1,2}$ = 8.6, $J_{2,3}$ = 10.6 Hz). In further synthesis, the minor component β-(XIII) can be used in a mixture with α-(XIII), or after its isomerization under acidic conditions into α-(XIII), but to simplify the spectral information, we used the α-(XIII) anomer.

The last compound was tranformed by oxidation by the method in [7] into aldehyde (XIV). Its PMR spectrum completely corresponds to the proposed structure ($J_{2,3}$ = 11 Hz, δ 9.84 ppm, s (CHO)). By reaction with $Ph_3P=CH_2$, aldehyde (XIV) was converted into the methylene derivative (XV). In its PMR spectrum, a set of well-resolved multiplets characteristic of the allyl system is present together with the signals of the tetrahydropyranyl part of the molecule. Hydrogenation of the double bond, carried out as before [8[by the action of a $LiAlH_4$–$CoCl_2$ mixture [9] leads to methyl-2,6,7-trideoxy-2,4-di-C-methyl-3,4,-di-O-benzyl-α-D-glucopyranoside (SVI), which is specficially protected C^9–C^{13} fragment of erythronolide A.

*The x-ray diffraction analysis was carried out by L. G. Vorontsova, and M. O. Dekaprilevich.

The methyl groups at C^2, C^4, and C^6 in the PMR spectrum of (XVI) appear in the form of signals with a characteristic multiplicity in the strong field (2-CH_3, 1.07 ppm, d, $J_{2\text{-}CH_3}$ = 6.5 Hz, 4-CH_3, 1.33 ppm, s; 6-CH_3, 1.02 ppm, t, $J_{6\text{-}CH_3}$ = 7.0 Hz). The SSCC $J_{1,2}$ = 3.6 and $J_{2,3}$ = 10.7 Hz correspond to the proposed orientation of the substituents at C^1, C^2, and C^3. Similarly, the SSCC $J_{5,6}$ = 10.4 and $J_{5,6'}$ = 1.8 Hz together with those for the predecessor compounds, confirm the axial orientation of the H^5 proton.

EXPERIMENTAL

The PMR and ^{13}C NMR spectra were run on a Bruker WM-250 spectrometer (in $CDCl_3$, internal standard TMS, δ = 0, J, Hz). The specific rotation was measured on a Perkin–Elmer M-141 pol polarimeter in $CHCl_3$. The TLC was carried on silica gel L (25-40 mμ) and the mixtures were separated on Silpearl silica gel (25-40 mμ) using continuous solvent gradients at an excess pressure of 0.5-1.2 atm.

1,6-Anhydro-2-dexoy-2-C-methyl-O-allyl-β-D-glucopyranose (VI). A 350-ml portion of a 1.0 M solution of Me_2Mg in ether (350 mmoles) [5] was added to 54.2 g (294 mmoles) of oxide (IV) in 200 ml of absolute ether. The mixture was boiled for 12 h. It was then decomposed by a saturated aqueous solution of NH_4Cl (35 ml). The precipitate was filtered and washed with ether, and the solution was dried over Na_2SO_4 and evaporated. The yield was 59.0 g (100%) of (VI) syrup, $[\alpha]_D^{23}$ −44.7° (C 1.13). PMR spectrum: 5.37 br. s (1H, H^1, $J_{1,2}$ = 1), 1.87 br. d (1H, H^2, $J_{2,3}$ = 1.5), 3.58 br. d (1H, H^3, $J_{3\text{-}OH}$ = 6), 3.37 br. s (1H, H^4), 5.59 br. d (1H, H^5, $J_{5,6\ endo}$ = 1), 4.10 br. d (1H, $H^{6,\ exo}$), 3.73 d.d. (1H, $H^{6\ exo}$, $J_{5,6\ exo}$ = 5.4, $J_{6,6'}$ = 7.3), 1.13 d (3H, 2-CH_3, $J_{2\text{-}CH_3}$ = 7.3), 2.72 br. d (1H, OH), 4.12 d.t, 5.21 d.q, 5.93 d.d.t (5H, $OCH_2CH{=}CH_2$). ^{13}C NMR spectrum: 104.6 (C^1), 41.3 (C^2), 71.3 (C^3), 79.6 (C^4), 74.7 (C^5), 65.4 (C^6), 14.9 (2-CH_3), 70.5 ($CH_2{=}CH\underline{CH_2}O$), 117.1 ($\underline{CH_2}{=}CHCH_2$), 134.7 ($CH_2{=}\underline{CH}CH_2O$).

1,6-Anhydro-2-dexosy-2-C-methyl-3-O-benzyl-4-O-allyl-α-D-glucopyranose (VII). A solution of 6.58 g (32.9 mmoles) of (VI) in 20 ml of absolute DMFA was stirred at 20°C for 1 h with 1.4 g (58.5 mmoles) of NaH. Then, 10 g (58.5 mmoles) of BnBr were added, and the mixture was stirred for another 30 min. Excess NaH was decomposed by MeOH, and the mixture was poured into water and extracted by ether. The extract was washed with water, and a saturated aqueous solution of NaCl, and evaporated, and the residue was chromatographed in a benzene–ethyl acetate (EA) gradient (0 → 25%). The yield of (VII) was 9.15 g (96%), syrup, $[\alpha]_D^{23}$ −32.9° (C 1.04). PMR spectrum: 5.31 br. s (1H, H^1, $J_{1,2}$ = 1), 2.0 br. q (1H, H^2), 3.30 m (1H, H^3, $J_{2,3}$ = $J_{3,4}$ = $J_{3,5}$ = 1.5), 3.36 br. s (1H, H^4), 5.56 br. d (1H, H^5), 4.14 d.d (1H $H^{6\ endo}$, $J_{5,6\ endo}$ = 1.3, $J_{6,6'}$ = 6.9), 3.74 d.d (1H, $H^{6\ exo}$, $J_{5,6\ exo}$ = 5.8), 4.53 d and 4.60 d (2H, AB spectrum $PhCCH_2O$), 4.02 d.t, 5.20 d.q, 5.27 d.w and 4.90 d.d.t (5H, $CH_2{=}CHCH_2O$). ^{13}C NMR spectrum: 104.1 (C^1), 37.9 (C^2), 78.2 (C^3), 77.6 (C^4), 74.5 (C^5), 64.9 (C^6), 15.7 (2-CH_3), 70.2 ($CH_2{=}CH\underline{CH_2}O$), 117.1 ($\underline{CH_2}{=}CHCH_2O$), 134.7 ($CH_2{=}\underline{CH}CH_2O$), 71.5 ($OCH_2Ph$).

1,6-Anhydro-2-desoxy-2-C-methyl-3-O-benzyl-β-D-glycopyranose (VIII). A solution of 8.83 g (30.4 mmoles) of (VII) and 8.33 g (74.5 mmoles) of t-BuOK in 45 ml of absolute DMSO was heated at 100°C for 1 h, and was then poured into water, and the mixture was extracted by $CHCl_3$. The extract was washed with water and a saturated solution of NaCl, and evaporated. The residue was dissovled in 300 ml of an acetone–water (10:1) mixture. A 6.6-g portion (30.5 mmoles) of HgO was added, and, with stirring, in the course of 5 min, a solution of 8.27 g (30.5 mmoles) of $HgCl_2$ in 100 ml of an acetone–water (10:1) mixture were added. The precipitate was filtered, the filtrate was evaporated, and the residue was diluted by water, and extracted by $CHCl_3$. The extract was washed with a 10% solution of KI, water, and a saturated solution of NaCl. It was then dried and evaporated, and the residue was chromatographed in a benzene–EA gradient (0 → 50%). The yield of (VIII) was 6.12 g (80), syrup, $[\alpha]_D^{24}$ −41.1° (C 1.06). PMR spectrum: 5.32 br. s (1H, H^1), 2.02 br. q (1H, H^2), 3.31 br. s (1H, H^3), 3.70 br. d (1H, H^4, $J_{4\text{-}OH}$ = 8.5), 4.48 br. d (1H, H^5, $J_{5,6\ exo}$ = 6), 4.23 br. d (1H, $H^{6\ endo}$, $J_{5,6\ endo}$ = 1, $J_{6,6'}$ = 7), 3.75 d.d (1H, $H^{6\ exo}$), 1.10 d (3H, 2-CH_3, $J_{2,\ CH_3}$ = 7.5), 4.57 br. s (1H, OH). 4.52 d and 4.59 d (AB spectrum OCH_2Ph, 2H, J_{gem} = 11.5). ^{13}C NMR spectrum: 104.4 (C^1), 37.3 (C^2), 80.6 (C^3), 70.5 (C^4), 76.3 (C^5), 64.7 (C^6), 16.4 (2-CH_3), 71.6 (OCH_2Ph).

1,6-Anhydro-2-desoxy-2-C-methyl-3-O-benzyl-β-D-xylohexapyranos-4-ylose (IX). A 17.3-ml portion of a 2.4 M solution of DMSO in absolute CH_2Cl_2 (40.5 mmoles) was added at −60°C, in the course of 5 min, to 34.5 ml of a 0.6 M solution of $(COCl)_2$ in absolute CH_2Cl_2 (20.7 mmoles). The mixture was stirred for 10 min, and a solution of 4.34 g (17.3 mmoles) of (VIII) in 15 ml of absolute CH_2Cl_2 was added. The mixture was stirred at −60°C for 15 min, 7 ml (50.4

mmoles) of Et_3N were added, and the cooling was stopped. The mixture was heated to 0°C in the course of 3-5 min, 30 ml of water were added, and the layers were separated. The aqueous layer was extracted by CH_2Cl_2. The extract was washed with 1 N HCl, saturated solutions of $NAHCO_3$ and NaCl, dried over over Na_2SO_4, and evaporated. The yield of (IX) was 4.24 g (98%), mp 66-66.5°C (ether—pentane), $[\alpha]_D^{24}$ +72.2° (C 1.3). PMR spectrum: 5.36 s (1H, H^1), 1.89 d. q (1H, H^2), 3.83 d (1H, H^3, $J_{2,3}$ = 7.6), 4.64 br. d (1H, H^5), 3.96 d.d (1H, H^6, endo, $J_{5,6}$ endo = 0.7, $J_{6,6'}$ = 7.2), 3.71 d.d (1H, H^6 exo, $J_{5,6}$ exo = 5.2), 1.21 d (3H, 2-CH_3, $J_{2,\ CH_3}$ = 7.2), 4.48 d and 4.92 d (2H, AB spectrum OCH_2Ph, J_{gem} = 11.2). ^{13}C NMR spectrum: 1.06.2 (C^1), 42.1 (C^2), 82.4 (C^3), 210.0 (C^4), 78.7 (C^5), 67.6 (C^6), 16.9 (2-CH_3), 73.8 ($PhCH_2O$).

1,6-Anhydro-2-desoxy-2-C-methyl-3-O-benzyl-4-methylene-β-D-xylopyranose (II). A 10.6-ml portion of a 1.8 M solution of n-BuLi in hexane (19.1 mmoles) was added to a suspension of 6.82 g (19.1 mmoles) of Ph_3PCH_3Br in 95 ml of absolute benzene. The mixture was stirred for 15 min, and heated to boiling, and 3.165 g (12.75 mmoles) of ketone(IX) in 15 ml of absolute benzene were added. The mixture was boiled for 10 min. Excess phosphorane was decomposed by acetone, the residue was filtered, and washed with benzene. The solution was evaporated and the residue was chromatographed in a benzene—ether gradient (0 → 10%). The yield of (II) was 2.62 g (84%), syrup, $[\alpha]_D^{21}$ −4.9°C (C 10.0). PMR spectrum: 5.0 d (1H, H^1, $J_{1,2}$ = 1.6), 2.2 d.d.dq. (1H, H^2), 3.53 d.d. (1H, H^3, $J_{2,3}$ = 1.3), 4.66 br. d (1H, H^5), 4.14 d.d. (1H, H^6 endo, $J_{5,6}$ endo = 0.8), 3.75 d.d (1H, H^6, exo, $J_{5,6}$ exo = 5.2, $J_{6,6'}$ = 6.7), 0.91 d (3H, $J_{2,\ CH_3}$ = 7.2; 4.28 d and 4.57 d (2H, AB spectrum OCH_2Ph, J_{gem} = 12), 5.24 d (1H, =CH), J_{gem} = 1.8), 5.29 d.d (1H, =CH), $J_{3,4'}$ = 1.3). ^{13}C NMR spectrum: 104.1 (C^1), 42.2 (C^2), 79.9 (C^3), 140.6 (C^4), 67.5 (C^6), 14.8 (2-CH_3), 69.6 ($PhCH_2O$), 117.7 (CH_2=).

1,6-Anhydro-2-desoxy-2,4-di-C-methyl-3-O-benzyl-β-D-gluco- (XI) and -galactopyranose (I). A soltuion of 1.05 g (4.26 mmoles) of (II) and 0.96 g of 80% m-chloroperbenzoic acid (5.02 mmoles) in 5 ml of $CHCl_3$ was boiled for 12 h, then decomposed by a saturated solution of Na_2SO_3, and themixture was extracted by $CHCl_3$. The extract was washed with water and a saturated solution of NaCl, dried over Na_2SO_4, and evaporated. The residue was dissolved in 2 ml of absolute THF, and 2 ml of a 1.18 M solution of $LiAlH_4$ in THF were added. After 10 min, excess hydride was decomposed by water, the mixture was diluted with $CHCl_3$, and filtered. The filtrate was washed with water and a saturated solution of NaCl, and evaporated. The residue was chromatographed in a benzene—ether gradient (0 → 25%). The yield of the galacto isomer (I) was 0.23 g (21%), mp 57-58°C pentane), $[\alpha]_D^{24}$ −88.9° (C 1.0), R_f 0.33 (benzene—ether, 3:1 [5]. The yield of the gluco isomer (XI) was 0.68 g (56%), syrup, $[\alpha]_D^{24}$ −87.0° (C 1.35), R_f 0.22 (benzene—ether, 3:1). PMR spectrum: 5.32 br. s (1H, H^1, $J_{1,2}$ = $J_{1,3}$ = 1), 2.07 br. q. (1H, H^2), 3.13 br. s (1H, H^3), 4.09 br. d (1H, H^5, $J_{5,6}$ exo = 5.5), 4.28 d.d (1H, H^6 endo, $J_{5,6}$ endo = 0.9, $J_{6,6'}$ = 6.8), 3.71 d.d (1H, H^6 exo), 1.12 d (3H, 2-CH_3, $J_{2,\ CH_3}$ = 7.4), 1.23 s (3H, 4-CH_3), 2.97 s (1H, OH), 4.37 d and 4.61 d (2H, AB spectrum $PhCH_2O$, J_{gem} = 11.0). NOE [4-CH_3], H^6 endo = 2.1%; [4-CH_3], H^5 = 2.6%; [4-CH_3], H^3 = 1.5%; [H^{6-endo}], 4-CH_3 = 5.7%. ^{13}C NMR spectrum: 104.2 (C^1). 37.4 (C^2), 83.2 (C^3), 72.0 (C^4), 49.9 (C^5) 63.9 (C^6), 16.8 (2-CH_3), 21.4 (4-CH_3), 72.1 ($PhCH_2O$).

1,6-Anhydro-2-desoxy-2,4-di-C-methyl-3,4-di-O-benzyl-β-D-glucopyranose (XII). A solution of 0.633 g (2.44 mmoles) of compound (XI) in 10 ml of absolute DMFA was stirred for 1 h with 0.3 g of NaH, then 0.82 g (4.8 mmoles) of BnBr were added, and the mixture was stirred for another 30 min. Excess NaH was decomposed by MeOH, the mixture was diluted with water, and extracted by $CHCl_3$. The extract was washed with water and a saturated solution of NaCl, dried over Na_2SO_4, and evaporated. The residue was chromatographed in a benzene—ether gradient (0 → 10%). The yield of (XII) was 0.817 g (96%), mp 100-100.5°C (ether—pentane), $[\alpha]_D^{23}$ −95.7° (C 0.9). PMR spectrum: 5.35 br. s (1H, H^1, $J_{1,2}$ = $J_{1,3}$ = 1), 2.05 br. q (1H, H^2), 3.27 br. s (1H, H^3, $J_{2,3}$ = 1), 4.45 br. d (1H, H^5), 4.27 d.d (1H, H^6 endo, $J_{5,7}$ endo = 1, $J_{6,6'}$ = 7), 3.75 d.d (1H, H^6, exo, $J_{5,6}$ exo = 5.5), 1.14 d (3H 2-CH_3, $J_{2,\ CH_3}$ = 7.5), 1.28 s (3H, 4-CH_3), 4.39 d and 4.63 d (2H, AB spectrum $PhCH_2O$, J_{gem} = 11.5), 4.41 d and 4.63 d (2H, AB spectrum $PhCH_2O$, J_{gem} = 10.2). ^{13}C NMR spectrum: 104.3 (C^1), 37.3 (C^2), 81.4 (C^3) 76.9 (C^4) 76.3 (C^5), 64.3 (C^6), 16.3 (2-CH_3), 17.6 (4-CH_3), 63.8 (4-$PhCH_2O$), 72.3 (3-$PhCH_2O$).

Methyl-2-desoxy-2,4-di-C-methyl-3,4-di-O-benzyl-D-glucopyranosides α-(XIII) and β-(XIII). A solution of 0.817 g (2.3 mmoles) of (XII) in 8 ml of a 20T solution of HCl in MeOH was held for 2 h at 20°C, then it was diluted with ether, and the mixture was neutralized by gaseous NH_3. Ammonium chloride was filtered, the precipitate was washed with ether, and the solution was evaporated. The residue was chromatographed in a benzene—ether gradient (0 → 25%), R_f = 0.32 (benzene—ether, 3:1) for α-(XIII), and 0.28 for β-(XIII). The yield of α-(XIII)

was 0.52 g (59%), mp 83-83.5°C (pentane), $[\alpha]_D^{22}$ +68.7° (C 1.2). PMR spectrum: 4.53 d (1H, H^1, $J_{1,2}$ = 3.5), 1.93 d.d.q (1H, H^2), 3.76 d (1H, H^3, $J_{2,3}$ = 11), 3.7-3.9 m (3H, H^5, H^6, $H^{6'}$, ABC spectrum), 1.08 d (3H, 2-CH_3, J_{2,CH_3} = 6.9), 1.37 s (3H, 4-CH_3), 2.12 br. s (1H, OH), 3.37 s (3H, MeO), 4.65 d and 4.77 d (2H, AB spectrum, 3-$PhCH_2O$, J_{gem} = 11), 4.72 s (2H, 4-$PhCH_2O$). ^{13}C NMR spectrum: 101.8 (C^1), 40.4 (C^2), 83.6 (C^3), 78.7 (C^4), 74.9 (C^5), 61.5 (C^6), 12.0 and 13.0 (2,4-CH_3), 54.9 (MeO), 65.6 (4-$PhCH_2O$), 72.4 (3-$PhCH_2O$).

The yield of β-(XIII) was 0.179 (20%), syrup. PMR spectrum: 4.11 d (1H, H^1, $J_{1,2}$ = 8.6), 1.79 d.d.q (1H, H^2), 3.36 d (1H, H^3, $J_{2,3}$ = 10.6), 3.51 d.d (1H, H^5, $J_{5,6}$ = 3.5, $J_{5,6'}$ = 7.5), 3.80 d.d (1H, H^6, $J_{6,6'}$ = 11.2), 3.95 d.d. (1H, $H^{6'}$), 1.1 d (3H, 2-CH_3, J_{2,CH_3} = 6.4), 1.42 s (3H, 4-CH_3), 2.3 br. s (1H, OH), 3.55 s (3H, MeO), 4.68 d and 4.83 d (2H, AB spectrum, 3-$PhCH_2O$, J_{gem} = 11.0), 4.68 d and 4.73 d (2H, AB spectrum, 4-$PhCH_2O$, J_{gem} = 11.0).

Methyl-2-desoxy-2,4-di-C-methyl-3,4-di-O-benzyl-6-aldo-α-D-glucopyranoside (XIV). A 2-ml portion of a 2.4 M solution of DMSO in absolute CH_2Cl_2 (4.8 mmoles) was added at −60°C, in the course of 10 min, to 4 ml of a 0.6 M solution of $(COCl)_2$ in absolute CH_2Cl_2 (2.4 mmoles). The mixture was stirred for 10 min, and then 0.762 g (1.97 mmoles) of α-(XIII) in 2 ml of absolute CH_2Cl_2 were added in the course of 10 min. The mixture was stirred at −60°C for 15 min, and then 0.82 g (6 mmoles) of Et_3N were added. Cooling was stopped, and the mixture was heated to 20°C. The mixture was diluted with CH_2Cl_2, washed with 1 N HCl and saturated solutions of $NaHCO_3$ and NaCl, and evaporated. The residue was chromatographed in the petroleum ether–ether (5:1) system. The yield of (XIV) was 0.628 g (83%), syrup, $[\alpha]_D^{22}$ +137.3° (C 1.18). PMR spectrum: 4.66 d (1H, H^1, $J_{1,2}$ = 3.5), 1.94 d.d.q (1H, H^2), 3.84 d (1H, H^3, $J_{2,3}$ = 10.5), 4.40 s (1H, H^5), 9.85 s (1H, CHO), 1.08 d (3H, 2-CH_3, J_{2,CH_3} = 6.5), 1.45 s (3H, 4-CH_3), 3.36 s (3H, MeO), 4.68 d and 4.82 d (2H, AB spectrum 3-$PhCH_2O$, J_{gem} = 11.0), 4.75 d and 4.81 d (2H, AB spectrum, 4-$PhCH_2O$, J_{gem} = 11.0).

Methyl-2,6,7-tridesoxy-2,4-di-C-methyl-3,4-di-O-benzyl-α-D-glucohept-6-enopyranoside (XV). A 1.4-ml portion of a 1.8 N solution of n-BuLi in hexane (2.5 mmoles) was added to a susepsnion of 0.892 g (2.5 mmoles) of Ph_3PCH_3Br in 15 ml of benzene. The mixture was stirred for 15 min, heated to boiling and a solution of 0.628 g (1.64 mmoles). of (XIV) in 3 ml of absolute benzene was added. After 20 min, excess phosphorane was decomposed by acetone, the solution was separated, the precipitate was extracted by hot benzene, and the solution was evaporated. The residue was chromatographed in a petroleum ether–ether (85:15) system. The yield of (XV) was 0.60 g (90%), syrup, $[\alpha]_D^{23}$ +81.8° (C 1.0). PMR spectrum: 4.56 d (1H, H^1 $J_{1,2}$ = 3.6), 1.95 d.dq (1H, H^2), 3.72 d (1H, H^3, $J_{2,3}$ = 10.6), 4.29 d.t (1H, H^5, $J_{5,6}$ = 5.4, $J_{5,7}$ = $J_{5,7'}$ = 1.5), 6.04 d.d.d (1H, H^6, $J_{6,7\text{-cis}}$ = 10.4, $J_{6,7\text{-trans}}$ = 17.0), 4.27 d.d.d (1H H^{7Z}, $J_{7,7'}$ = 2), 5.44 d.d. (1H, E-H^7), 1.06 d (3H, 2-CH_3, J_{2,CH_3} = 6.6) 1.36 s (3H, 4-CH_3), 3.32 s (3H, MeO), 4.62 d and 4.80 d (2H, AB spectrum 3-$PhCH_2O$, J_{gem} = 11), 4.66 d and 4.70 d (2H, AB spectrum 4-$PhCH_2O$, J_{gem} = 11).

Methyl-2,6,7-tridesoxy-2,4-di-C-methyl-3,4-di-O-benzyl-α-D-glucoheptapyranoside (XVI). A 0.8-g portion of a 1.18 M solution of $LiAlH_4$ in THF was added at −40°C, in the course of 15 min, to a mixture of 0.395 g (1.03 mmoles) of (XV) and 0.133 g (1.03 mmoles), of $CoCl_2$ in 5 ml of absolute THF. After 5 min, the mixture was decomposed by a few drops of water, diluted with $CHCl_3$, washed with water and a saturated solution of NaCl, and evaporated. The residue was chromatographed in the petroleum ether–ether (9:1) system. The yield of (XVI) was 0.315 g (80), syrup, $[\alpha]_D^{22}$ +74.7° (C 0.95. PMR spectrum: 4.50 d (1H, H^1, $J_{1,2}$ = 3.6), 1.94 d.d.q (1H, H^2), 3.72 d (1H, H^3, $J_{2,3}$ = 10.7), 3.65 d.d. (1H, H^5, $J_{5,6}$ = 10.4, $J_{5,6'}$ = 1.8), 1.44 d.d.q (1H, H^6,$J_{6,6'}$ = 13.5), 1.28 d.d.q (1H, $H^{6'}$), 1.07 d (3H, 2-CH_3, J_{2,CH_3} = 6.5), 1.33 s (3H, 4-CH_3), 1.02 t (3H, 6, CH_3, J_{6,CH_3} = 7), 3.35 s (3H, MeO), 4.62 d and 4.80 d (2H, AB spectrum, 3-$PhCH_2O$, J_{gem} = 11), 4.66 d and 4.70 d (2H, AB spectrum, 4-$PhCH_2O$, J_{gem} = 11). ^{13}C NMR spectrum: 101.7 (C^1), 40.3 (C^2), 83.5 (C^3), 79.4 (C^4), 74.9 (C^5), 21.2 (C^6), 11.4 and 11.6 (2-CH_3, C^7), 13.1 (4-CH_3), 65.3 (4-$PhCH_2O$), 73.9 (3-$PhCH_2O$).

Methyl-2-desoxy-2,4-di-C-methyl-3-O-benzyl-D-glucopyranosides α-(XVII) and β-(XVII). A solution of 0.258 g (0.98 mmole) of (XI) in 10 ml of a 20% solution of HCl in MeOH was held at 10°C for 40 min, and then was diluted with dry ether. The mixture was neutralized by gaseous NH_3, NH_4Cl was filtered, and the solution was evaporated. The residue was chromatographed in a benzene–EA gradient (10 → 50%). The yield of (XVII) was 0.153 g (53%), syrup, $[\alpha]_D^{23}$ +96.3° (C 1.03). PMR spectrum: 4.51 d (1H, H^1, $J_{1,2}$ = 3.5), 1.82 d.d.q (1H, H^2), 3.43 (1H, H^3, $J_{2,3}$ = 11), 3.60-3.90 m (3H, H^5, H^6, $H^{6'}$, ABC spectrum), 1.03 d (3H, 2-CH_3, J_{2,CH_3} = 6.5), 1.21 s (3H, 4-CH_3), 2.73 and 2.93 br. s (2H, 4OH, 6-OH), 3.32 s (3H, MeO), 4.68 d and 4.80 d (2H, AB spectrum, 3-$PhCH_2O$, J_{gem} = 11).

The yield of (XVIII) was 0.077 g (27%), mp 96.5-97°C (ether—pentane) $[\alpha]_D^{23}$ −8.4° (C 1.12). PMR spectrum: 4.03 d (1H, H^1, $J_{1,2}$ = 8.5), 1.64 d.d.q (1H, H^2), 3.07 d (1H, H^3, $J_{2,3}$ = 10.7), 3.32 d.d. (1H, H^5, $J_{5,6}$ = 5.5, $J_{5,6'}$ = 6.5), 3.77 d.d. (1H, H^6, $J_{6,6'}$ = 11), 3.88 d.d (1H, H^6), 1.04 d (3H, 2-CH_3; J_{2,CH_3} = 6.5), 1.24 s (3H, 4-CH_3), 3.49 s (3H, MeO), 2.80 and 2.92 br. s (2H, 4-OH, 6-OH), 4.71 d and 4.86 d (2H, AB spectrum 3-$PhCH_2O$, J_{gem} = 11).

Methyl-2-desoxy-2,4-di-C-methyl-3-O-benzyl-6-O-mesyl-α-D-glucopyranoside (XIX). A 0.065-g portion (0.57 mmole) of MsCl in 0.5 ml of CH_2Cl_2 was added, with cooling to −10°C and stirring, in the course of 5 min to a solution of 0.141 g (0.475 mmole) of (XVII) in 2 ml of CH_2Cl_2 and 0.072 g (0.71 mmole) of Et_3N. Stirring was continued for 10 min and the mixture was poured into a 1 N solution of HCl. The mixture was extracted by $CHCl_3$, and the extract was washed with saturated solutions of $NaHCO_2$ and NaCl, and dried over Na_2SO_4 and evaporated. The residue was chromatographed in a benzene—ether gradient (10 → 25%). The yield of (XIX) was 0.16 g (90%), syrup. PMR spectrum: 4.55 d (1H, H^1, $J_{1,2}$ = 3.5), 1.88 d.d.q (1H, H^2), 3.43 d (1H, H^3, $J_{2,3}$ = 11), 3.87 d.d. (1H, H^5, $J_{5,6}$ = 8.5, $J_{5,6'}$ = 2), 4.27 d.d (1H, H^6, $J_{6,6'}$ = 10.5), 4.57 d.d (1H, H^6), 1.07 d (3H, 2-CH_3, J_{2,CH_3} = 7), 1.18 s (3H, 4-CH_3), 1.92 br. s (1H, 4-OH), 3.02 s (3H, 6-$MeSO_3$), 3.35 s (3H, MeO), 4.70 d and 4.77 d (2H, AB spectrum 3-$PhCH_2O$, J_{gem} = 11).

A 0.16-g portion (0.425 mmole) of (XIX) in 1 ml of THF was added at −5°C to a solution of Me_2CuLi, prepared from 0.35 g (1.7 mmoles) of $CuBr \cdot Me_2S$ in 5 ml of absolute ether and 3.78 ml of a 0.9 N MeLi solution (3.4 mmoles). The mixture was stirred at 0°C for 2 h, and was then decomposed by a saturated solution of NH_4Cl. The mixture was extracted by $CHCl_3$, and the extract was washed with a saturated solution of NaCl, dried over Na_2SO_4, and evaporated. The residue was chromatographed in a benzene—EA gradient (25 → 50%). The yield of (XVII) was 0.113 g (90).

CONCLUSIONS

1. An effective scheme of synthesis of 1,6-anhydro-2-desoxy-2-C-methyl-3-O-benzyl-4-methylene-β-D-xylohexapyranose, an important intermediate compound in the synthesis of macrolide antibiotics, has been developed.

2. A C^9—C^{13} fragment of erythronolide A was synthesized in 14 stages from levoglucosan to give an overall yield of 7.5%.

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