hexane–EA (8:1) system. Yield, 0.269 g (78%), syrup, $[\alpha]_D^{20} = -11.4°$ (C 1.0). PMR spectrum (δ, ppm, J, Hz): 0.92 t (3H, CH_3CH_2), 1.1 d (3H, $J_{4,Me}$ = 7, Me at C^4), 1.38 s (3H, Me at C^2), 1.5 d.d (1H, $J_{3,3'}$ = 14, $J_{3,4}$ = 3, H^3), 2.44 m (3H, $CH_3\underline{CH_2}$, H^3), 2.85 d.d.q (1H, $J_{3,4}$ = 9.5, H^4), 4.42 s (2H, $Ph\underline{CH_2}O$), 7.35 m (5H, $\underline{Ph}CH_2O$), 9.52 s (1H, H^1).

CONCLUSIONS

A synthesis of a C^5-C^9-fragment common to erythronolides A and B was carried out starting from levoglucosan.

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SYNTHESIS OF MACROLIDE ANTIBIOTICS.

17.* SYNTHESIS OF THE C^1-C^{10}-FRAGMENT OF ERYTHRONOLIDES (A) AND (B)

A. F. Sviridov, V. S. Borodkin,
M. S. Ermolenko, and D. V. Yashunskii

UDC 542.91:547.455

In the preceding article, the strategy was discussed of the stereodirected synthesis of erythronolides A and B in the sequence of coupling the $(C^5$-$C^9)$ + $(C^3$-$C_4)$ + $(C^1$-$C^2)$ + (C^{10}) + $(C^{11}$-$C^{13})$ fragments and also the synthesis of the C^5-$C^{9\dagger}$ fragment, the aldehyde (I), was described. The subject of the present article is the synthesis of the C^1-C^{10} fragment, the ketone (XX), from aldehyde (I).

It was proposed to carry out the extension of the C^1-C^4 fragment of the carbon chain and construction of the sequence of the C^2-C^5 chiral centers on transition from (I) to (XX) by adding tri-n-butylcrotyltin (TBCT) to aldehydes (I) and (XVI) in the presence of Lewis acids. The possibility of controlling the stereochemical result of this type of transformation by selecting the reaction promoters and suitable protecting groups in the substrates was demonstrated on the model of chiral α- and β-alkoxyaldehydes [2, 3].

Magnesium bromide $MgBr_2$ was chosen as a promoter for the addition of TBCT to aldehyde (I) [2], since the presence of an α-benzyloxy group in the molecule of the substrate opened up the possibility of the α-chelation of aldehyde (I) in the transition state, whereby the

*For previous communication, see [1].
†The numbering of the carbon atoms in the compounds described in the present article corresponds to the numbering of the erythronolide B carbon chain.

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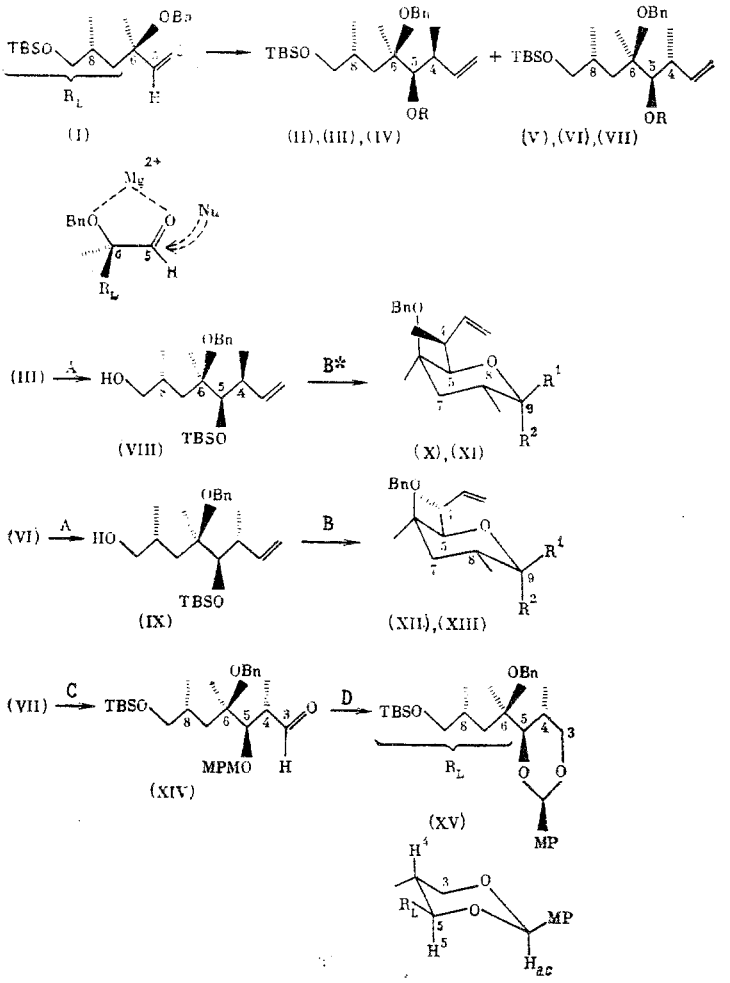
attack on the reagent from the direction of the smaller substituent should lead to the formation of the "natural" configuration of the C^5 center (scheme 1).

Scheme 1



R = H (II); TBS (III); MPM (IV); R = H (V); TBS (VI), MPM (VII); R^1 = H, R^2 = OMe (X); R^1 = OMe, R^2 = H (XI); R^1 = H, R^2 = OMe (XII); R^1 = OMe, R^2 = H (XIII)
A. AcOH–THF $-H_2O$ (6:3:1); B. 1) $(COCl)_2$, DMSO, $Et_3N-CH_2Cl_2$, −60°; 2) 3% HCl—MeOH; C. $O_3-CH_2Cl_2$/Py, −78°; D. 1) $LiAlH_4-Et_2O$, −40°; 2) DDQ—CH_2Cl_2, molecular sieves 3Å.

In fact, in the reaction of aldehyde (I) with TBCT in the presence of $MgBr_2$ a (4:1) mixture of homoallyl alcohols (II) and (V), respectively, is formed. To establish the configuration of the C^5 center, after the chromatographic separation, compounds (II) and (V) were subjected to a transformation of the same type. Silylation of (II) and (V) at the secondary hydroxyl group and the subsequent selective removal of the primary tert-butyldimethylsilyl (TBS) protective group under carefully selected conditions of acid hydrolysis (AcOH:THF:H_2O, 6:3:1) lead to primary alcohols (VIII) and (IX). Oxidation of these compounds and treatment of the aldehydes obtained with 3% HCl in MeOH gives chromatographically separable mixtures of methylglycosides (X) + (XI) and (XII) + (XIII), respectively.

The SSCC ($J_{9,8}$ = 3.25, $J_{8,7a}$ = 12.5 Hz) in the PMR spectrum of compound (X) and ($J_{9,8}$ = 8, $J_{8,7a}$ = 12 Hz) in the spectrum of (XI) show that the two compounds are present in the $^4C_1$-conformation, whereby the H^9 proton in (X) is equatorial, while in (XI) it is axial. The presence of nuclear electrostatic repulsion (NER) on the H^9 proton (6.2%) in (XI) during preirradiation of the H^5 proton indicates the steric convergence of these protons, i.e., their 1,3-syn-diaxial orientation. At the same time, in compound (X), on the H^9 proton, the NER is not observed during the preirradiation of the H^5 proton.

All of the above spectral data unequivocally confirm a D-configuration of the C^5 center in methylglycosides (X) and (XI), corresponding to the "natural" configuration of the C^5 center in the homoallyl alcohol (II).

In the pair of methylglycosides (XII) and (XIII), a diaxial orientation of the H^5 and H^9 protons was established for compound (XIII), which, considering the $^4C_1$-conformation of compounds (XII) and (XIII), indicates the D-configuration of the C^5 centers also in this pair of compounds.

Thus, the addition of TBCT to aldehyde (I) proceeds with exclusively diastereophase selectivity: the C^5 center in the homoallyl alcohols (II) and (V) has the "natural" conformation, while the difference between these compounds is determined by the configuration of the C^4 center.

It was found for the minor product (V) that in the cyclic derivative (XV), obtained from (V) in 4 stages (scheme 1), the SSCC value ($J_{4,5}$ = 9.5 Hz) corresponds to the anti-configuration of the C^4 and C^5 centers, and therefore a syn-configuration of these centers was assigned to compound (II), which was later confirmed experimentally. The homoallyl alcohol having a confirmed "natural" configuration of the C^4 and C^5 center was used in the further synthesis.

In the reaction of TBCT with β-silyloxyaldehyde (XVIa) in the presence of $BF_3 \cdot Et_2O$, the predominant reaction product is compound (XVIIa) with a "nonnatural" configuration* of the C^3 center. This unexpected result† is probably the consequence of the specific conformation of the reacting aldehyde (XVIa) due to the structural complexity of the molecule (Scheme 2).

By altering the character of the protecting group of hydroxyl at C^5, it was possible to obtain the 2,3,4-syn-homoallyl alcohol (XVII) in 70% yield‡ in the reaction of aldehyde (XVI) [obtained from (II) in two stages] with TBCT in the presence of $BF_3 \cdot Et_2O$ (cf. [4]). Treatment of (XVII) with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in absolute CH_2Cl_2 [5] gives the cyclic 3,5-O-p-methoxybenzylideneacetal (XVIII) in the form of a single isomer with respect to the acetal center. All the spectral data ($J_{3,4} = J_{4,5}$ = 1.5 Hz, NER [H^{α}], H^5 = 6.5%, H^3 = 7.5%) unequivocally determine the required syn-configuration of the C^3, C^4, and C^5 centers in (XVIII). The configuration of the C^2 center was not determined at this stage of the synthesis, but was confirmed later.

The conversion of derivative (XVIII) with the "natural" configuration of the C^2-C^5 centers into ketone (XX) completes the synthesis of the C^1-C^{10} fragment of erythronolides A and B. In the reaction of (XVIII) with an acetone–dimethoxypropane mixture containing an equimolar amount of $TsOH \cdot H_2O$, as a result of the removal of the 9-O-TBS protecting group and trans-acetation of the 3,5-diol system, alcohol (XIX) is formed in almost quantitative yield. This compound was converted into ketone (XX) by a standard sequence of operations, including oxidation, addition of EtMgBr to the aldehyde obtained and repeated oxidation of the secondary alcohols (see scheme on following page).

The use of ketone (XX) in the synthesis of erythronolides A and B will be discussed in the succeeding articles.

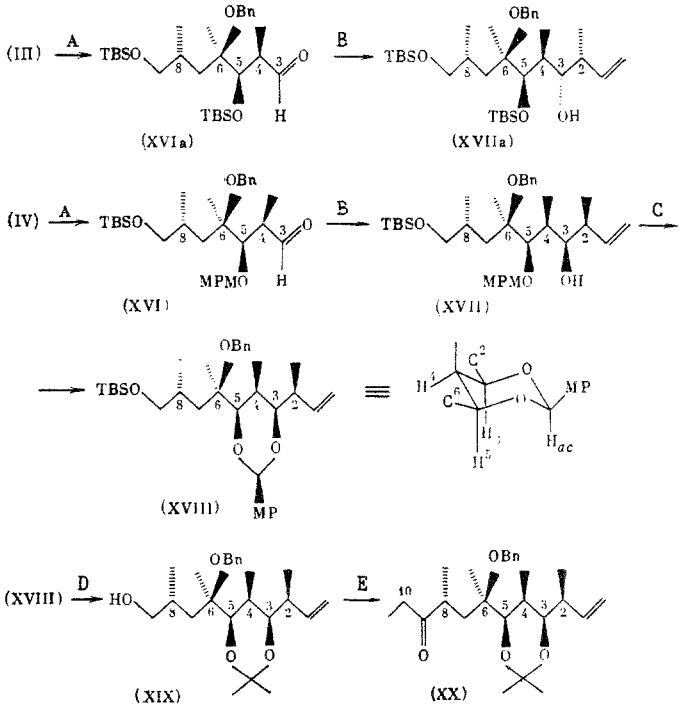
EXPERIMENTAL

The PMR spectra were taken in $CDCl_3$ solutions on a Bruker WM-250 spectrometer. The specific optical rotation was measured on a Perkin–Elmer M-141 polarimeter in $CHCl_3$. The course of the reactions was monitored by the TLC on plates with silica gel from E. Merck. The compounds were purified and the reaction mixtures were separated by the HPLC method on a column with a Silpearl silica gel (25-40 μm).

The absolute solvents were prepared by distillation in an argon atmosphere over appropriate drying agents, directly before use. Benzene, pyridine, hexane, diisopropylamine, DMSO, and triethylamine were distilled over CaH_2. Ether and THF were held over alkali and

*This configuration was established from examination of the PMR spectrum of the corresponding 3,5-O-isopropylidene derivative.
†Compare the result of the addition of TBCT to the model β-siloxyaldehydes [3].
‡All the four possible diastereomers are formed. Overall yield 90%.

Scheme 2



A. O_3—CH_2Cl_2/Py, —78°; B. $MgCH{=}CHCH_2SnBu_3$; $BF_3{\cdot}Et_2O$—CH_2Cl_2, —78°; C. DDQ—CH_2Cl_2, molecular sieves 3 Å.; D. DMP, Me_2CO—$TsOH{\cdot}H_2O$; E. 1) $(COCl)_2$, DMSO, Et_3N—CH_2Cl_2, —60°; 2) EtMgBr—THF, —50°; 3) $(COCl)_2$, DMSO, Et_3N—CH_2Cl_2, —60°.

distilled over $LiAlH_4$. Methylene chloride CH_2Cl_2 was distilled first over P_2O_5, and then over powdered CaH_2.

Compounds (II) and (V). A solution of 0.821 g (2.3 mmoles) of aldehyde (I) in 6 ml of CH_2Cl_2 added to 0.508 g of $MgBr_2$ and then 1 ml (2.54 mmoles) of tri-n-butylcrotyltin (TBCT) was added, and the mixture was stirred for 50 h at 20°C. The mixture was decomposed by water and extracted with $CHCl_3$ (2 × 15 ml). The extract was washed with water and a saturated solution of NaCl, dried over Na_2SO_4, evaporated, and the residue was chromatographed in a hexane—ether (5%) system. The yield of (II) was 0.6 g (64%), syrup, $[\alpha]_D^{20}$ = +8.6° (C 0.5); (V), 0.141 g (13%), syrup, $[\alpha]_D^{20}$ +5.4° (C 4.85). PMR spectrum of (II) (δ, ppm, J, Hz): 0.06 s [6H, $\underline{Me}_2$(t-BuSiO)], 0.93 s [9H, Me_2(t-$\underline{Bu}$SiO)], 1.01 d ($J_{4,Me}$ = 6.5, Me at C^4), 1.14 d (3H, $J_{8,Me}$ = 6.5 Me at C^8), 1.3 s (3H, Me at C^6), 1.55 d.d (1H, $J_{7',7}$ = 14.5, $J_{7,8}$ = 7.5, H^7), 1.85 d.d (1H $J_{7',8}$ = 3.2, $H^{7'}$), 1.9 m (1H, H^8), 2.45 d.d.q (1H, H^4), 3.4 (2H, AB-system, H^9, $H^{9'}$), 3.63 d (1H, $J_{4,5}$ = 5, H^5), 4.5 (2H, AB-system, J_{gem} = 10.5, $Ph\underline{CH}_2O$), 4.99 d.d (1H, $J_{3°\,cis,\,3}$ = 10, $J_{3°\,cis,\,3°\,trans}$ = 1.7, $H^{3°}$ cis), 5.4 br. d.d (1H, $J_{3°\,trans,\,3}$ = 16.5, $H^{3°}$ trans), 5.9 d.d.d multiplet center (1H, $J_{3,4}$ = 8 Hz, H^3), 7.35 m (5H, $C_6\underline{H}_5CH_2O$). PMR spectrum of (V) (δ, ppm, J, Hz): 0.05 s [6H, $\underline{Me}_2$(t-BuSiO)], 0.9 s [9H, Me_2(t-$\underline{Bu}$SiO)], 0.99 d (3H, $J_{8,Me}$ = 6.5, Me at C^8), 1.19 d (3H, $J_{Me,\,4}$ = 7, Me at C^4), 1.27 s (3H, Me at C^6), 1.43 d.d (1H, $J_{7',7}$ = 15.5, $J_{7,8}$ = 8.5, H^7), 1.83 d.d (1H, $J_{7',8}$ = 3.2, H^7), 1.85 m (1H, H^8), 2.51 multiplet center (2H, H^4, OH), 3.39 and 3.43, multiplet centers (2H, AB part of ABX spectrum, J_{gem} = 9.5, H^9, $H^{9'}$), 4.63 br.s (1H, H^5), 4.46 multiplet center (2H, AB-spectrum, J_{gem} = 11, $Ph\underline{CH}_2O$), 5.02 multiplet center (2H, AB part of ABMX system, $H^{3°c}$, $H^{3°t}$), 6.06 multiplet center (1H, M-part of ABMX system, H^3), 7.35 m (5H, $C_6\underline{H}_5CH_2O$).

Compound (III). A 30 μliters portion (0.226 mmole) of Et_3N was added to a solution of 23 mg (0.056 mmole) of (II) in 1 ml of CH_2Cl_2. The mixture was cooled to —20°C and 25 μliters (0.113 mmole) of TBSOTf were added. The mixture was stirred for 1 h, brought to room temperature, decomposed by a $NaHCO_3$ solution, and extracted with $CHCl_3$. The extract was washed with water, 1 N HCl solution, and a standard solution of NaCl, dried over Na_2SO_4, evaporated, and the residue was chromatographed in a hexane—ether (1%) system. Yield,

29 mg (98%) syrup, $[\alpha]_D^{20}$ −9.3° (C 1.5). PMR spectrum (δ, ppm, J. Hz): 0.01 two s [6H, $\underline{Me}_2$(t-BuSiO)], 0.05 d [6H, $\underline{Me}_2$(t-BuSiO)], 0.88 s [9H, Me_2(t-$\underline{Bu}$SiO)], 0.92 s [9H, Me_2(t-$\underline{Bu}$SiO)], 0.97 d (3H, $J_{Me,8}$ = 6.7 Me at C^8), 1.02 d (3H, $J_{Me,4}$ = 7, Me at C^4), 1.31 s (3H, Me at C^6), 1.47 d.d (1H, $J_{7',7}$ = 15, $J_{7,8}$ = 6.2, H^7), 1.66 d.d (1H, $J_{7',8}$ = 5, $H^{7'}$), 1.9 m (1H, H^8), 2.77 m (1H, H^4), 3.29 d.d (1H, $J_{9',9}$ = 10, $J_{8,9}$ = 7.5, H^9), 3.61 d.d (1H, $J_{8,9'}$ = 5.7, $H^{9'}$), 3.8 d (1H, $J_{4,5}$ = 1.5, H^5), 4.4 d and 4.52 d (2H, AB-system, J_{gem} = 11, $Ph\underline{CH}_2O$), 4.97 multiplet center (2H, J_{trans} = 17, J_{cis} = 10, $H^{3°}$ trans, $H^{3°}$ cis), 5.93 d.d.d (1H, $J_{3,4}$ = 7.5, H^3), 7.3 m (5H, $C_6\underline{H}_5CH_2O$).

Compound (VI) was obtained in a similar way as (III), syrup, $[\alpha]_D^{20}$ −11.3° (C 4.65). PMR spectrum (δ, ppm, J, Hz): 0.05 s, 0.03 s, 0.09 s [12H, $\underline{Me}_2$(t-BuSiO)], 0.9 s [18H, Me_2(t-$\underline{Bu}$SiO)], 0.97 d (3H, $J_{Me,8}$ = 6.5, Me at C^8), 1.11 d (3H, $J_{Me,4}$ = 7.5, Me at C^4), 1.24 s (3H, Me at C^6), 1.46 d.d (1H, $J_{7',7}$ = 15, $J_{7,8}$ = 7.5, H^7), 1.71 d.d (1H, $J_{7',8}$ = 4, $H^{7'}$), 1.83 m (1H, H^8), 2.66 br.d.q (1H, H^4), 3.33 d.d (1H, $J_{9',9}$ = 10, $J_{8,9}$ = 6.2, H^9), 3.45 d.d.d (1H, $J_{8,9'}$ = 6.2, $H^{9'}$), 3.75 d (1H, $J_{4,5}$ = 1, H^5), 4.39 d and 4.5 d (2H, AB-system, $C_6H_5C\underline{H}_2O$), 4.94 and 5.0 multiplet centers (2H, AB-part of ABMX spectrum, $H^{3°}$ cis, $H^{3°}$ trans), 6.07 m (1H, M part of ABMX spectrum, H^3), 7.3 m, 5H, $C_6\underline{H}_5CH_2O$).

Compound (IV). A solution of 0.6 g (1.48 mmoles) of (II) in 3 ml of DMF was added to a suspension of 70 mg of NaH in 3 ml of DMF. The mixture was stirred for 1 h at 20°C, 430 μliter (3 mmoles) of 4-methoxybenzyl chloride were added, and the mixture was allowed to stand overnight. The mixture was decomposed with MeOH, and after adding water, was extracted with ether (3 × 20 ml). The extract was washed with water and a saturated solution of NaCl, dried over Na_2SO_4, evaporated, and the residue was chromatographed in a hexane–ether (3.5%) system. Yield, 0.76 g (97.4%), syrup, $[\alpha]_D^{20}$ −29° (C 1.0). PMR spectrum (δ, ppm, J, Hz): 0.00 s [6H, $\underline{Me}_2$(t-BuSiO)], 0.88 s [9H, Me_2(t-$\underline{Bu}$SiO)], 0.99 d (3H, $J_{Me,4}$ = 6.7, Me at C^4), 1.15 d (3H, $J_{Me,8}$ = 7, Me at C^8), 1.36 s (3H, Me at C^6), 1.45 d.d (1H, $J_{7',7}$ = 14.5, $J_{7,8}$ = 6, H^7), 1.7 d.d (1H, $J_{7',8}$ = 5.5, $H^{7'}$), 1.92 m (1H, H^8), 2.74 m (1H, H^4), 3.28 d.d (1H, $J_{9',9}$ = 9.7, $J_{8,9}$ = 7.5, H^9), 3.55 d (1H, $J_{4,5}$ = 3, H^5), 2.62 d.d (1H, $J_{8,9'}$ = 5.5, $H^{9'}$), 3.83 s (3H, $\underline{Me}OC_6H_4CH_2O$), 4.5 m (2H, AB-spectrum J_{gem} = 11, $MeOC_6H_4$-$C\underline{H}_2O$), 4.57 m (2H, AB-spectrum, J_{gem} = 11, $C_6H_5C\underline{H}_2O$), 4.93 d.d.d. (1H, $J_{3°cis,3}$ = 10, $J_{3°cis,4}$ = 1.5, J_{gem} = 1.5, $H^{3°}$cis), 5.0 d.d.d (1H, $J_{3°trans,3}$ = 17, $J_{3°trans,4}$ = 1.5, $H^{3°}$trans), 5.98 d.d.d (1H, $J_{3,4}$ = 7.5, H^3), 6.89 and 7.3 m (9H, aromatic protons).

Compound (VII) was obtained in a 75% yield in a similar way as (IV), syrup, $[\alpha]_D^{20}$ −30.7° (C 1.75). PMR spectrum (δ, ppm, J, Hz): 0.06 s [6H, $\underline{Me}_2$(t-BuSiO)], 0.92 s [9H, Me_2(t-BuSiO)], 1.02 d (3H, $J_{Me,8}$ = 6.5, Me at C^8), 1.18 d (3H, $J_{Me,4}$ = 6.7 Me at C^4), 1.36 s (3H, Me at C^6), 1.46 d.d. (1H, $J_{7',7}$ = 1.5, $J_{7,8}$ = 7.5, H^7), 1.75 d.d (1H, $J_{7',8}$ = 4, $H^{7'}$), 1.87 m (1H, H^8), 2.67 m (1H, H^4), 3.37 d.d (1H, $J_{9',9}$ = 10, $J_{8,9}$ = 6.5, H^9), 3.5 d.d (1H, $J_{8,9'}$ = 6, H^9), 3.54 d (1H, $J_{4,5}$ = 1.8, H^5), 3.83 s (3H, $\underline{Me}OC_6CH_4CH_2O$), 4.49 d and 4.55 d (2H, AB-spectrum, $Ph\underline{CH}_2O$), 4.6 d and 4.8 d (2H, AB-spectrum $MeOPh\underline{CH}_2O$), 4.98 d.d (1H, $J_{3°cis,3}$ = 10, $H^{3°}$cis), 5.03 d.d (1H, $J_{3°trans,3}$ = 17, $H^{3°}$trans), 6.1 d.d.d (1H, $J_{3,4}$ = 8.5, H^3), 6.89 m, 7.3 (9H, aromatic protons).

Compound (VIII). A 23 mg portion of (III) was dissolved in 5 ml of a THF–AcOH–H_2O (3:6:1) mixture. The mixture was held for 2 h at 50°C, and then for 12 h at 20°C, was then neutralized with a saturated solution of $NaHCO_3$, and extracted with $CHCl_3$. The extract was washed with water and a saturated NaCl solution, dried over Na_2SO_4, evaporated, and the residue was chromatographed in a hexane–EA (13%) system. Yield, 14 mg, (77%), syrup, $[\alpha]_D^{20}$ −12° (C 4.0). PMR spectrum (δ, ppm, J, Hz): 0.1 d [6H, $\underline{Me}_2$(t-BuSiO)], 0.93 d (3H, $J_{Me,8}$ = 7, Me at C^8), 0.95 s [9H, Me_2(t-BuSiO)], 1.03 d (3H, $J_{Me,4}$ = 7, Me at C^4), 1.4 s (3H, Me at C^6), 1.58 d.d (1H, $J_{7',7}$ = 14.5, $J_{7,8}$ = 9, H^7), 1.76 d.d (1H, $J_{7',8}$ = 3, $H^{7'}$), 1.9 m (1H, H^8), 2.88 m (1H, H^4), 3.28 m (2H, H^9, OH), 3.58 m (1H, $H^{9'}$), 3.87 d (1H, $J_{4,5}$ = 1.8, H^5), 4.41 d and 4.5 d (2H, AB spectrum, J_{gem} = 11, $C_6H_5C\underline{H}_2O$), 4.99 m (2H, $J_{3°trans,3}$ = 17 Hz, $J_{3°cis,3}$ = 10, $J_{3°trans,4}$ = 1.5, $H^{3°}$cis, $H^{3°}$trans), 5.91 d.d.d (1H, $J_{3,4}$ = 7.7, H^3), 7.32 m (5H, $C_6\underline{H}_5CH_2O$).

Compound (IX) was obtained in a similar way as (VIII), syrup, $[\alpha]_D^{20}$ −13.6° (C 3.5). PMR spectrum (δ, ppm, J, Hz): 0.01 s and 0.045 s [6H, $\underline{Me}_2$(t-BuSiO)], 0.93 d (3H, $J_{Me,8}$ = 7, Me at C^8), 0.95 s [9H, Me_2(t-BuSiO)], 1.14 d (3H, $J_{Me,4}$ = 7.2, Me at C^4), 1.36 s (3H,

Me at C^6), 1.62 d.d (1H, $J_{7',7}$ = 15, $J_{7,8}$ = 4.5, H^7), 1.72 d.d (1H, $J_{7',8}$ = 7.5, $H^{7'}$), 1.87 m (1H, H^8), 2.85 br.d.q (1H, H^4), 3.27 d.d (1H, $J_{9',9}$ = 10.5, $J_{8,9}$ = 6.7, H^9), 3.52 d.d ($J_{8,9'}$ = 4.2, $H^{9'}$), 3.8 d (1H, $J_{4,5}$ = 1, H^5), 4.42 d and 4.53 d (2H, AB-spectrum, $Ph\underline{CH_2}O$), 5.0 m (2H, J_{trans} = 17, J_{cis} = 10, $H^{3°t}$, $H^{3°c}$), 6.6 d.d.d (1H, $J_{3,4}$ = 8, H^3), 7.35 m (5H, $C_6\underline{H_5}CH_2O$).

Compounds (X) and (XI). A solution of 77 mg (0.18 mmole) of (VIII) in 1 ml of CH_2Cl_2 was added at −60°C to a solution of the Swern reagent, obtained from 87 μliters (1 mmole) of $(COCl)_2$ and 141 μliters (2 mmoles) of DMSO in 2.5 ml of CH_2Cl_2. The mixture was stirred for 25 min and 0.55 ml (4 mmoles) of Et_3N was added. The mixture was heated to 0°C, and after adding 5 ml of 1 N HCl, was diluted with $CHCl_3$. The extract was washed with water and a saturated solution of NaCl, dried over Na_2SO_4 and evaporated. The residue was dissolved in 1.5 ml of a 3% HCl solution in MeOH, the solution was allowed to stand for 12 h and was then neutralized by saturated solution of $NaHCO_3$. The mixture was extracted with $CHCl_3$ (2 × 25 ml), the extract was dried over Na_2SO_4, evaporated, and the residue was chromatographed in a hexane–ether (7%) system. Yield 40 mg (73%), the α/β ratio = 1:2. α-Anomer (X), syrup, $[\alpha]_D^{20}$ +67.6° (C 0.9). PMR spectrum (δ, ppm, J, Hz): 4.55 d (1H, $J_{9,8}$ = 3.2, H^9), 2.12 m (1H, H^8), 1.44 d.d (1H, $J_{7\alpha,7e}$ = 14, $J_{7\alpha,8}$ = 12.5, $H^{7\alpha}$), 1.85 d.d. (2H, $J_{7e,8}$ = 4, H^{7e}), 3.47 d (1H, $J_{5,4}$ = 4.5, H^5), 2.77 m (1H, H^4), 5.93 d.d.d (1H, $J_{3,4}$ = 8, H^3), 4.93 d.d.d (1H, $J_{3°cis,3}$ = 10, J_{gem} = 2.1, $J_{3°cis,4}$ = 0.5, $H^{3°cis}$), 5.04 d.d.d (1H, J_{trans} = 17, $J_{3°trans,4}$ = 1.7, $H^{3°trans}$), 3.36 s (3H,MeO), 0.87 d (3H, $J_{Me,8}$ = 6.7, Me at C^8), 1.2 d (3H, $J_{Me,4}$ = 6.5, Me at C^4), 1.23 s (3H, Me at C^6), 4.41 d and 4.5 d (2H, AB spectrum, $Ph\underline{CH_2}O$), 7.35 m (5H, $C_6\underline{H_5}CH_2O$). β-Anomer (XI), syrup, $[\alpha]_D^{20}$ −37.8° (C 0.73). PMR spectrum (δ, ppm, J, Hz): 3.93 d (1H, $J_{8,9}$ = 8.2, H^9), 1.9 m (1H, H^8), 1.07 d.d (1H, $J_{7',7}$ = 14, $J_{7\alpha,8}$ = 12, $H^{7\alpha}$), 2.1 d.d (1H, $J_{7e,8}$ = 4, H^{7e}), 3.15 d (1H, $J_{4,5}$ = 4.7, H^5), 2.82 m (1H, H^4), 5.91 d.d.d (1H, $J_{3,4}$ = 8.2, H^3), 4.91 d.d (1H, J_{cis} = 10, J_{gem} = 2, $H^{3°cis}$), 5.03 d.d.d (1H, J_{trans} = 17, $J_{3°\,trans,4}$ = 1), 3.5 s (3H,MeO), 0.9 d (3H, $J_{Me,8}$ = 6.5, Me at C^8), 1.19 d and 1.21 s (6H, $J_{Me,4}$ = 6.5, Me at C^4 and C^6), 4.45 s (2H, A_2-spectrum $Ph\underline{CH_2}O$), 7.32 m (5H, $C_6\underline{H_5}CH_2O$). NER: $[H^5]$, H^9 = 6.2%; $[H^5]$, H^4 = 13%.

Compounds (XII) and XIII) were obtained in a similar way as (X) and (XI). α-Anomer (XII), syrup, $[\alpha]_D^{20}$ −58.5° (C 1.0). PMR spectrum (δ, ppm, J, Hz): 4.57 d (1H, $J_{8,9}$ = 3.5, H^9), 2.16 m (1H, H^8), 1.42 d.d (1H, $J_{7',7}$ = 14, $J_{7\alpha,8}$ = 13, $H^{7\alpha}$), 1.85 d.d (1H, $J_{7e,8}$ = 4, H^{7e}), 3.48 d (1H, $J_{4,5}$ = 2.5, H^5), 1.76 m (1H, H^4), 6.36 d.d.d (1H, $J_{3,4}$ = 7, H^3), 4.95 m (2H, J_{trans} = 17, J_{cis} = 10, J_{gem} = $J_{3,3°trans}$ = $J_{3,3°cis}$ = 2, $H^{3°trans}$, $H^{3°cis}$), 3,39 s (3H, MeO), 0.86 d (3H, $J_{Me,8}$ = 7, Me at C^8), 1.12 d (3H, $J_{Me,4}$ = 7, Me at C^4), 1.23 s (3H, Me at C^6), 4.38 d and 4.47 d (2H, AB spectrum, $Ph\underline{CH_2}O$), 7.35 m (5H, $C_6\underline{H_5}CH_2O$). NER: $[H^5]$, H^4 = 4.1%; $[H^5]$, $H^{7\alpha}$ = 3.6%. β-Anomer (XIII), syrup, $[\alpha]_D^{20}$ −43° (C 1.0). PMR spectrum, (δ, ppm, J, Hz): 3.92 d (1H, $J_{8,9}$ = 8.5, H^9), 1.91 m (1H, H^8), 1.05 d.d (1H, $J_{7',7}$ = 15, $J_{7\alpha,8}$ = 12.5, $H^{7\alpha}$), 2.1 d.d (1H, $J_{7e,8}$ = 4, H^{7e}), 3.12 d (1H, $J_{4,5}$ = 3, H^5), 2.75 m (1H, H^4), 6.29 d.d.d (1H, $J_{3,4}$ = 8, H^3), 4.91 m (2H, J_{trans} = 17, J_{cis} = 10 Hz, $H^{3°trans}$, $H^{3°cis}$), 3.5 s (3H, MeO), 0.91 d (3H, $J_{Me,8}$ = 6.7 Hz, Me at C^8), 1.81 d (3H, $J_{Me,4}$ = 7, Me at C^4), 1.2 s (3H, Me at C^6), 4.43 s (A_2-spectrum, $Ph\underline{CH_2}O$), 7.3 (5H, $C_6\underline{H_5}CH_2O$). NER: $[H^5]$, H^9 = 5%.

Compound (XIV). A 7 ml portion of pyridine and 10.5 ml of 0.05% solution of the Sudan (IV) dye in CH_2Cl_2 were added to a solution of 0.365 g (0.67 mmole) of (VII) in 0.6 liter of CH_2Cl_2. The mixture was ionized at −60 to −80°C to the disappearance of the indicator's color. The solution was purged with argon at −75°C for 20 min. The temperature was brought to 20°C in the course of 1.5 h, the solvent was evaporated, and traces of pyridine were evaporated in the form of azeotrope with heptane. The residue was chromatographed in a hexane–ether system (15%). Yield 0.275 g (75%), syrup, $[\alpha]_D^{20}$ −29° (C 1.0). PMR spectrum (δ, ppm, J, Hz): 0.02 s [6H, $\underline{Me}_2$(t-BuSiO)], 0.9 s [9H, Me_2(t-BuSiO)], 1.0 d (3H, $J_{Me,8}$ = 6.5, Me at C^8), 1.22 d (3H, $J_{Me,4}$ = 7, Me at C^4), 1.4 s (3H, Me at C^6), 1.54 d.d (1H, $J_{7',7}$ = 14, $J_{7,8}$ = 6.2, H^7), 1.81 d.d (1H, $J_{7',8}$ = 4.5, $H^{7'}$), 1.9 m (1H, H^8), 2.9 d.d.q (1H, H^4), 3.32 d.d (1H, $J_{9',9}$ = 9.5, $J_{8,9}$ = 6.5, H^9), 3.57 d.d (1H, $J_{8,9'}$ = 5.5, $H^{9'}$), 3.68 d (1H, $J_{4,5}$ = 2, H^5), 3.82 s (3H, $\underline{Me}OPhCH_2O$), 4.5 d and 4.56 d (2H, AB-spectrum, $Ph\underline{CH_2}O$), 4.56 d and 4.65 d (2H, AB-spectrum, $p\text{-}MeOC_6H_4\underline{CH_2}O$), 6.89 m and 7.3 m (9H aromatic protons), 9.85 d (1H, $J_{3,4}$ = 2.5, H^3).

Compound (XV). A solution of 26 mg (0.05 mmole) of (XIV) in 1 ml of ether was treated with excess $LiAlH_4$ at −40°C, stirred for 20 min, heated to 20°C, and decomposed by successive addition of 100 μliters of water, 100 μliters of 15% NaOH solution and 300 μliters of water. The mixture was filtered, the precipitate was washed with ether, and the filtrate was evaporated. The residue was dissolved in 1 ml of CH_2Cl_2, 80 mg of molecular sieves 3 Å and 20 mg (0.075 mmole) of DDQ were added, the mixture was stirred for 30 min, decomposed with a saturated solution of $NaHCO_3$, and extracted with $CHCl_3$ (2 × 25 ml). The extract was washed with water and a saturated solution of NaCl, dried over Na_2SO_4, evaporated, and the residue was chromatographed in a hexane–ether (12%) mixture. Yield 23 mg (88%), syrup, $[\alpha]_D^{20}$ −21.1° (C 4.4). PMR spectrum (δ, ppm, J, Hz): 0.014 s [6H, $\underline{Me}_2$(t-BuSiO)], 0.9 s [9H, Me_2(t-BuSiO)], 0.95 d (3H, $J_{Me,4}$ = 6.5, Me at C^4), 1.0 d (3H, $J_{Me,8}$ = 6.5, Me at C^8), 1.43 s (3H, Me at C^6), 1.57 d.d (1H, $J_{7',7}$ = 14, $J_{7,8}$ = 5, H^7), 1.75 d.d (1H, $J_{7',8}$ = 6.5, $H^{7'}$), 1.97 m (1H, H^8), 2.2 m (1H, H^4), 3.3 d.d (1H, $J_{9',9}$ = 9.5, $J_{8,9}$ = 7.5, H^9), 3.5 d.d (1H, $J_{3\alpha,3e}$ = 11, $J_{3\alpha,4}$ = 11, $H^{3\alpha}$), 3.65 d (1H, $J_{4,5}$ = 9.5, H^5), 3.75 d.d (1H, $H_{8,9'}$ = 5, H^9), 3.82 s (3H, $\underline{Me}$OPhCH=), 4.06 d.d (1H, $J_{3e,4}$ = 4.5, H^{3e}), 4.52 d and 4.62 d (2H, AB-spectrum, Ph$\underline{CH_2}$O), 5.46 s (1H, H of an acetal), 6.9 m and 7.35 m (9H, aromatic protons).

Compound (XVI) was obtained in a similar way as (XIV). Yield 73%, syrup, $[\alpha]_D^{20}$ −27.6° (C 0.5). PMR spectrum, (δ, ppm, J, Hz): 0.01 s [6H, $\underline{Me}_2$(t-BuSiO)], 0.88 s [9H, Me_2(t-BuSiO)], 0.98 d (3H, $J_{Me,8}$ = 6.6, Me at C^8), 1.26 d (3H, $J_{Me,4}$ = 7.2, Me at C^4), 1.4 (3H, Me at C^6), 1.49 d.d (1H, $J_{7',7}$ = 15, $J_{7,8}$ = 5.5, H^7), 1.63 d.d (1H, $J_{7',8}$ = 6, $H^{7'}$), 1.91 m (1H, H^8), 2.92 d.d.q (1H, H^4), 3.26 d.d (1H, $J_{9',9}$ = 9.6, $J_{8,9}$ = 7.5, H^9), 3.63 d.d. (1H, $J_{8,9'}$ = 5.5, $H^{9'}$), 3.82 s (3H, $\underline{Me}$OPhCH$_2$O), 4.05 d (1H, $J_{4,5}$ = 3.9, H^5), 4.45 m (4H, Ph$\underline{CH_2}$O, MeOPh$\underline{CH_2}$O), 6.9 m and 7.3 m (9H, aromatic protons), 9.64 d (1H, $J_{3,4}$ = 1.5, H^3).

Compound (XVII). A 34 μliter portion (0.275 mmole) of $BF_3 \cdot Et_2O$ was added at −78°C to a solution of 97 mg (0.18 mmole) of (XVI) in 1 ml of CH_2Cl_2. The mixture was stirred for 5 min and 160 μliters (0.4 mmole) of TBCT was added, and the mixture was stirred for 45 min. It was then decomposed by 1.5 ml of a saturated solution of NH_4Cl, and heated to 20°C, diluted with 20 ml of water, and extracted with $CHCl_3$ (2 × 10 ml). The extract was washed with water and a saturated solution of NaCl, dried over Na_2SO_4, evaporated, and the residue was chromatographed in a hexane–ether (4:1) system. Yield 78 mg, syrup, $[\alpha]_D^{20}$ −6° (C 0.25). PMR spectrum (δ, ppm, J, Hz): 0.035 s [6H, $\underline{Me}_2$(t-BuSiO)], 0.9 s [9H, Me_2(t-BuSiO)], 0.96 d (3H, $J_{Me,8}$ = 6.7, Me at C^8), 1.0 d (3H, $J_{Me,2}$ = 6.5, Me at C^2), 1.04 d (3H, $J_{Me,4}$ = 6.7, Me at C^4), 1.4 s (3H, Me at C^6), 1.44 d.d (1H, $J_{7',7}$ = 15, $J_{7,8}$ = 6.7, H^7), 1.68 d.d (1H, $J_{7',8}$ = 4, $H^{7'}$), 1.87 m (1H, H^3), 2.15 d.d.q (1H, $J_{3,4}$ = 2, H^4), 2.28 d.d.q (1H, $J_{2,3}$ = 8.5, H^2), 3.33 d.d (1H, $J_{9',9}$ = 9.5, $J_{8,9}$ = 6.7 Hz, H^9), 3.5 d.d (1H, $J_{8,9'}$ = 6, $H^{9'}$), 3.47 br.d (1H, H^2), 3.69 d (1H, $J_{4,5}$ = 3.5, H^5), 3.8 s (3H, $\underline{Me}$OPhCH$_2$O), 4.53 s (2H, A_2-spectrum, Ph$\underline{CH_2}$O), 4.61 d and 4.82 d (2H, AB-spectrum, J_{gem} = 11, MeOPh$\underline{CH_2}$O), 4.96 d.d (1H, J_{cis} = 10, J_{gem} = 2, $H^{1°cis}$), 5.04 d.d (1H, J_{trans} = 17, $H^{1°trans}$), 5.57 d.d.d (1H, $J_{1,2}$ = 9, H^1), 6.87 and 7.3 m (9H, aromatic protons).

Compound (XVIII). A 100 mg portion of molecular sieves 3 Å and 33 mg (0.14 mmole) of DDQ was added to a solution of 78 mg (0.13 mmole) of (XVII) in 1 ml of CH_2Cl_2. The mixture was stirred for 30 min, was then decomposed with a saturated solution of Na_2SO_3, filtered through celite, and the precipitate was washed with $CHCl_3$. The filtrate was washed with water and saturated solutions of $NaHCO_3$ and NaCl, dried over Na_2SO_4, evaporated and the residue was chromatographed in a hexane–ether (5%) system. Yield 63 mg (81%), syrup, $[\alpha]_D^{20}$ −14.8° (C 2.0). PMR spectrum, (δ, ppm, J, Hz): 0.01 s [6H, $\underline{Me}_2$(t-BuSiO)], 0.94 s [9H, Me_2(t-BuSiO)], 1.07 d (3H, $J_{Me,8}$ = 6.6, Me at C^8), 1.18 two d (6H, $J_{Me,2}$ = $J_{Me,4}$ = 6.5, Me at C^2 and C^4), 1.4 s (3H, Me at C^6), 1.4 d.d (1H, $J_{7,7'}$ = 15, $J_{7,8}$ = 7.5, H^7), 1.94 m (3H, H^4, H^8, $H^{7'}$), 2.54 d.d.q (1H, H^2), 3.38 d.d (1H, $J_{9',9}$ = 10, $J_{8,9}$ = 7, H^9), 3.45 d.d (1H, $J_{2,3}$ = 10, $J_{3,4}$ = 2, H^3), 3.56 d.d (1H, $J_{8,9'}$ = 6, H^9), 3.83 d (1H, $J_{4,5}$ = 2, H^5), 3.5 s (3H, $\underline{Me}$OPhCH$_2$O), 4.74 m (2H, AB-spectrum, J_{gem} = 12, Ph$\underline{CH_2}$O), 5.1 d.d (J_{cis} = 10, J_{gem} = 2, $H^{1°cis}$), 5.19 d.d (1H, J_{trans} = 17, $H^{1°trans}$), 5.47 s (1H, H_{ac}, MeOPh$\underline{CH}$=), 6.95 m and 7.51 m, 7.3 m (9H, aromatic protons), NER: [H_{ac}], H^5 = 6.5%; [H_{ac}], H^3 = 7.5%.

Compound (XIX). A 66 mg portion (0.35 mmole) of $TsOH \cdot H_2O$ was added to a solution of 0.205 g (0.35 mmole) of (XVIII) in 5 ml of a dimethoxypropane–acetone (1:1) mixture. The

mixture was allowed to stand for 12 h, then was poured into a saturated $NaHCO_3$ solution, and was extracted by $CHCl_3$ (2 × 20 ml). The extract was washed with water and a saturated solution of NaCl, dried over Na_2SO_4, evaporated, and the residue was chromatographed in hexane–EA (12%) mixture. Yield 0.13 g (95%), syrup, $[\alpha]_D^{20}$ +16.6° (C 4.75). PMR spectrum (δ, ppm, J, Hz): 0.937 d (3H, $J_{Me,4}$ = 6 Me at C^4), 0.96 d (3H, $J_{Me,8}$ = 6.8, Me at C^8), 1.05 d (3H, $J_{Me,2}$ = 6.5, Me at C^2), 1.34 d.d (1H, $J_{7',7}$ = 14.5, $J_{7,8}$ = 11, H^7), 1.4 s, 1.42 s, 1.45 s (9H, Me at C^6, Me_2C=), 1.65 d.d.q (1H, $J_{3,4}$ = 2, H^4), 1.71 d.d (1H, $J_{7',8}$ = 14.5, $H^{7'}$), 2.0 m (1H, H^8), 2.32 d.d.q (1H, $J_{2,3}$ = 10, H^2), 3.25 br.d.d (1H, H^9), 3.45 d.d (1H, $J_{3,4}$ = 2, H^3), 5.25 br.d.d (1H, H^9), 3.99 d (1H, $J_{4,5}$ = 2, H^5), 4.6 d and 4.75 d (2H, AB-spectrum, J_{gem} = 11, $PhC\underline{H}_2O$), 5.0 d.d (1H, J_{cis} = 10, J_{gem} = 2, $H^{1°}cis$), 5.11 d.d (1H, J_{trans} = 17.5 ($H^{1°}trans$), 5.59 d.d.d (1H, $J_{1,2}$ = 8.5, H^1), 7.3 m [5H, ($C_6\underline{H}_5CH_2O$)].

Compound (XX). A solution of 188 μliters (2.66 mmoles) of DMSO in 1 ml of CH_2Cl_2 was added at −60°C to a solution of 116 μliters (1.33 mmoles) of ($COCl_2$) in 2 ml of CH_2Cl_2. After 15 min, a solution of 130 mg of (XIX) in 2 ml of CH_2Cl_2 was added, the mixture was held for 25 min and 742 μliters (5.3 mmoles) of Et_3N were added, and the reaction mixture was allowed to stand for 10 min at −10°C. The mixture was heated in the course of 1 min to 0°C, 6 ml of 1 N HCl solution and 20 ml of water were added, and the mixture was extracted with $CHCl_3$. 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 THF, the solution was cooled to −40°C, excess of EtMgBr in THF was added, and the mixture was allowed to stand for 30 min. The mixture was heated to 20°C and decomposed with a saturated solution of NH_4Cl. The precipitate was filtered and washed with ether, and the filtrate was evaporated. The residue was oxidized under the above-described conditions and with the same amounts of the reagents. The material was chromatographed in a hexane–ether (9:1) system. Yield, 108 mg (78%), syrup, $[\alpha]_D^{20}$ +22.3° (C 1.0). PMR spectrum, (δ, ppm, J, Hz): 0.66 t (3H, Me at C^{10}), 0.94 d (3H, $J_{Me,4}$ = 7, Me at C^4), 1.03 d (3H, $J_{Me,2}$ = 6.5, Me at C^2), 1.06 d (3H, $J_{Me,8}$ = 7, Me at C^8), 1.27 d.d (1H, $J_{7',7}$ = 14, $J_{7,8}$ = 2.5, H^7), 3.5 two s, 4.25 s (9H, Me at C^6, Me_2C=), 1.66 d.d.q (1H, H^4), 2.12 d.q (1H, $J_{10',10}$ = 18, H^{10}), 2.33 m (3H, $J_{7',8}$ = 9, H^{10}, $H^{7'}$, H^2), 2.8 d.d.q (1H, H^8), 3.44 d.d (1H, $J_{3,4}$ = 2, H^3), 3.92 d (1H, $J_{4,5}$ = 2, H^5), 4.47 d and 4.61 d (2H, AB-spectrum, J_{gem} = 11, $PhC\underline{H}_2O$), 5.04 d.d (1H, J_{cis} = 10, J_{gem} = 2, $H^{1°}cis$), 5.1 d.d (1H, J_{trans} = 17, $H^{1°}trans$) 5.6 d.d.d (1H, $J_{1,2}$ = 8.5, H^1), 7.25 m (5H, $C_6\underline{H}_5CH_2O$).

CONCLUSIONS

A synthesis of the C^1-C^{10} fragment of erythronolides (A) and (B) with a reliably established configuration of the C^3-C^6 and C^8 centers has been carried out.

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