methylene), 66.85, 70.74, 71.79, 73.43, 73.63, 75.82, (C2, C4, C5, C6, C7, C8), 80.61 ($C(CH_3)_3$), 109.32 ($C(CH_3)_2$), 168.85, 172.78 (carbonyls). Anal. Calcd for $C_{22}H_{36}O_9$: C, 59.44; H, 8.16. Found: C, 59.2; H, 8.2.

Methyl 2,6-Anhydro-2-benzyl-3-deoxy-4,5:7,8-di-*O*-isopropylidene-D-*glycero*-D-*galacto*- and -D-*talo*-octonate (20a and 20b). Benzyl bromide (0.25 mL, 2.1 mmol) in anhydrous THF (5 mL) was added to the enolate (prepared from 300 mg of a mixture of **7a** and **7b**; 0.95 mmol) at −75 °C. After 30 min the solution was warmed to room temperature and saturated NH_4Cl solution (5 mL) was added. The mixture was extracted with ether. The extract was dried (Na_2SO_4) and concentrated, yielding a syrup which was purified on a silica gel column with ether/pentane (2:1) as eluent. Syrupy **20a** (<10 mg) and crystalline **20b** (230 mg, 64%) were obtained. **20a**: ^1H NMR ($CDCl_3$) δ 1.20, 1.27, 1.35 (3s, 12 H, isopropylidene methyls), 1.78 (dd, 1 H, $J_{3ax,3eq}$ = −15.4, $J_{3ax,4}$ = 2.9, H3ax), 2.77 (dd, 1 H, $J_{3eq,4}$ = 4.7, H3eq), 2.88 (br s, 2 H, CH_2), 3.26 (dd, 1 H, $J_{6,7}$ = 9.4, $J_{6,5}$ = 2, H6), 3.48 (s, 3 H, OMe), 4.0–4.3 (m, H5, H7, H8, H8′), 4.45 (ddd, 1 H, $J_{4,5}$ = 7.7, H4), 7.18 (s, 5 H, aromatic). **20b**: mp 63–66 °C; $[\alpha]_D$ −18.0° (*c* 1.6, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.37, 1.55 (2s, 12 H, isopropylidene methyls), 1.88–2.28 (m, 2 H, $J_{3ax,4}$ = 4.5, $J_{3eq,4}$ = 4.5, H3ax, H3eq), 3.20 (dd, 2 H, methylene), 3.33 (dd, 1 H, $J_{6,7}$ = 8.2, $J_{6,5}$ = 1.2, H6), 3.53 (s, 3 H, OMe), 3.85–4.45 (m, 4 H, H5, H7, H8, H8′), 4.50 (ddd, 1 H, $J_{4,5}$ = 7.1, H4), 7.0–7.2 (m, 5 H, aromatic); ^{13}C NMR ($CDCl_3$) δ 25.32, 27.02 (isopropylidene methyls), 31.56 (C3), 46.56 (methylene), 51.75 (OMe), 67.10 (C8), 70.89, 71.69, 73.93, 74.03 (C4, C5, C6, C7), 79.36 (C2), 109.27 (overlapping signals, $C(CH_3)_2$), 126.77, 127.92, 130.26, 135.95 (aromatic), 173.53 (C1). Anal. Calcd for $C_{22}H_{30}O_7 \cdot {}^1/_4H_2O$: C, 64.30; H, 7.48. Found: C, 64.4; H, 7.5.

Ethyl 2,6-Anhydro-3-deoxy-4,5:7,8-di-*O*-isopropylidene-2-[2-(methoxycarbonyl)ethyl]-D-*glycero*-D-*galacto*- and -D-*talo*-octonate (21a and 21b). Methyl acrylate (95 mg, 1.11 mmol) dissolved in 1 mL of anhydrous THF was added to the enolate (prepared from 310 mg of **22**; 0.94 mmol) at −75 °C. The reaction mixture was stirred for 1 h before saturated NH_4Cl solution (1.5 mL) was added. The mixture was allowed to reach room temperature and dried (Na_2SO_4). After filtration and concentration the syrupy residue was purified on a silica gel column with ether/pentane (3:1) as eluent, giving 30 mg (8%) of pure **21a**, a mixture of **21b**, **22**, and an unidentified compound. **21a**: $[\alpha]_D$ −0.8° (*c* 1.3, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.20–1.50 (15 H, isopropylidene methyls, ethyl ester methyl), 1.71 (d, 1 H, $J_{3ax,3eq}$ = −15.1, $J_{3ax,4}$ = 2.6, H3ax) 1.85–2.96 (m, 4 H, -CH_2CH_2-), 2.79 (d, 1 H, $J_{3eq,4}$ = 2.6, H3eq), 3.34 (dd, 1 H, $J_{6,5}$ = 1.6, $J_{6,7}$ = 5.8, H6), 3.66 (s, 3 H, OMe) 3.85–4.40 (m, 6 H, H5, H7, H8, H8′, ethyl ester methylene), 4.51 (ddd, 1 H, $J_{4,5}$ = 8, H4); ^{13}C NMR ($CDCl_3$) δ 14.21 (ethyl ester methyl), 24.62, 25.02, 25.22, 26.97, 27.96, 32.40, 33.70 (-CH_2CH_2-, isopropylidene methyls, C3), 51.74 (OMe), 61.17 (ethyl ester methylene), 67.20 (C8), 69.89, 72.08, 72.33, 74.93, 75.77 (C2, C4, C5, C6, C7), 109.12, 109.52 ($C(CH_3)_2$), 172.78, 173.33 (carbonyls). Anal. Calcd for $C_{20}H_{32}O_9 \cdot H_2O$: C, 55.28; H, 7.92. Found: C, 55.3; H, 7.6.

Acknowledgment. We thank Miss K. Crona for skillful technical assistance and Miss A. Jansson and Mr H. Molin for providing help with 200-MHz NMR spectra. We also thank Dr. B. Pring for linguistic corrections. This work was supported by the National Swedish Board for Technical Development.

Registry No. **2**, 73508-80-2; **3**, 73650-00-7; **4**, 66053-63-2; **5a**, 109150-72-3; **5b**, 107573-27-3; **6a**, 109150-73-4; **6b**, 106174-63-4; **7a**, 107961-77-3; **7b**, 109150-74-5; **8**, 85382-90-7; **9b**, 109150-75-6; **10**, 109150-83-6; **11**, 109150-84-7; **12**, 109150-85-8; **13**, 109150-86-9; **14a**, 109150-79-0; [^{13}C]-**14a**, 109150-81-4; **14b**, 109150-80-3; [^{13}C]-**14b**, 109150-82-5; **14b** (benzyl ether), 109150-87-0; **15a**, 109150-77-8; **15b**, 109150-78-9; **16a**, 109150-88-1; **16b**, 109150-89-2; **17b**, 109150-90-5; **18a**, 109150-92-7; **18b**, 109150-91-6; **19b**, 109150-93-8; **20a**, 109150-94-9; **20b**, 109150-95-0; **21a**, 109150-96-1; **21b**, 109150-97-2; **22** (isomer 1), 109150-76-7; **22** (isomer 2), 109150-98-3; PhOAc, 122-79-2; AcCl, 75-36-5; Ac_2O, 108-24-7; HC≡CH_2Br, 106-96-7; $BrCH_2COOBu$-*t*, 5292-43-3; H_2C=CHCOOMe, 96-33-3.

Practical Synthesis of Diastereomerically and Enantiomerically Pure 2-Methyl 1,3-Diols from (*R*)-2,3-*O*-Isopropylideneglyceraldehyde. Application to the C(1)–C(7) and C(9)–C(12) Fragments of Erythronolide B

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The synthesis of the homochiral 2-methyl 1,3-diol derivatives **1**, **2**, and **3** from (*R*)-2,3-*O*-isopropylideneglyceraldehyde via **4**/**5a–e** is described. **1** and **2** are prepared from **4**/**5b** via the epoxides **6**/**7**, which are opened regiospecifically by the Lipshutz methylcuprate reagent at C-2. **3** is obtained from **4e** via the epoxide **12**, which is converted into **13** by a Payne rearrangement and then treated with the cuprate. **1** corresponds to the C(9)–C(12) segment of erythronolide B; furthermore, **17b**, containing the C(1)–C(7) segment of erythronolides A and B, is prepared from **2c** via **18a**/**b** as intermediates.

The synthesis of propionate-derived macrolide antibiotics is one of the most attractive topics in current organic chemistry. In view of the notorious complexity of the target structures, the following three-step strategy appears to be appropriate.[1] (1) Construction of stereochemically defined 2-methyl 1,3-diol subunits (A) with differentiable functional groups FG^1 and FG^2 at both ends. (2) Elaboration of A into larger substructures. (3) Combining these substructures into the desired target molecule.

A wide variety of methods has been developed to prepare A in diastereomerically and frequently also in enantiomerically pure form, for instance, aldoltype condensations and variations thereof,[2] olefination–hydroboration[3]

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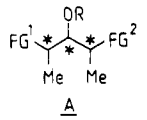
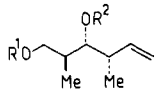


A



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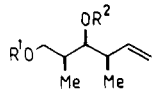

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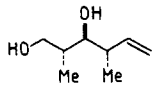
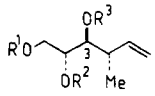


3

1, 2	R^1	R^2
a	H	H
b	Tr	H
c	Tr	Bn

or olefination–hydrosilylation,[4] cuprate ring opening of epoxides,[5] hetero-Diels–Alder reactions,[6] oxymercuration of cyclopropylcarbinols,[7] reduction of 1,3-ketols,[8] and [2 + 2]-cycloaddition of dichloroketene to a chiral olefin with subsequent Bayer–Villiger oxidation.[9] Additionally, derivatives of type A have been obtained from D-glucose,[10a] (*S*)-glutamic acid, D-ribonolactone, or D-mannitol,[10b] or by enzymatic partial hydrolysis of a mesodiacetate.[11]

We report the synthesis of compounds **1**, **2**, and **3** in multigram quantities from the optically and diastereomerically pure triol derivatives **4a**/**5a**, which are readily



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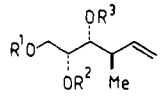
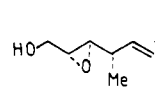


5

4, 5	R^1	R^2	R^3
a	$-CMe_2-$		H
b	$-CMe_2-$		Ts
c	H	H	Ts
d	H	H	H
e	Ts	H	H

available[12] from (*R*)-2,3-*O*-isopropylideneglyceraldehyde. On parallel routes **4a** and **5a** were transformed via **4**/**5b,c** into the epoxy alcohols **6** and **7**, which on treatment with Lipshutz' methylcuprate[13] regiospecifically[5] furnished the 1,3-diol derivatives **1a**/**2a** in about 40% overall yield. The configurations of **1a**/**2a**, though being clear from the course of the synthesis, were independently secured by conversion into the known[10,16c] triacetates **8**/**9**. As expected, **9** proved to be a meso compound with an optical rotation near zero and isochronous ^{13}C NMR signals for C-1/5, 2/4, and 6/7, whereas **8** exhibited a specific rotation of $[\alpha]^{20}_D$ −3.19° ($CHCl_3$) and showed clearly separated signals for the above-mentioned carbons in the ^{13}C NMR spectrum. The ^1H NMR spectra of **8** and **9** were identical with those reported in the literature.[10,16c] With respect to future applications the two hydroxy functions in **1a**/**2a** were protected differently by first tritylating the primary OH group and then benzylating the secondary one to obtain **1b**/**2b** and **1c**/**2c**, respectively. **1b** and **2b** have been converted into **10** and **11** by a Mitsunobu reaction,[15] thus enhancing the versatility of these key intermediates.



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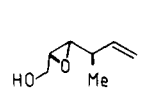

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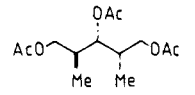

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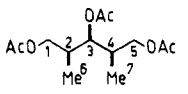

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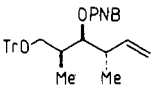

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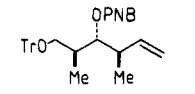
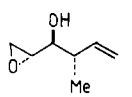


11

The synthesis of **3** from **4a** required retention at C-3, which invoked the application of a Payne rearrangement.[14] Hence, **4a** was first hydrolyzed and then monotosylated to furnish the crystalline primary tosylate **4e**, which on treatment with methoxide was converted into either one of the two epoxides **12** and **13** by merely varying the solvent. In methanol, only **12** was formed, whereas in chloroform **13** was the sole product under identical conditions. Cuprate ring opening of **13** yielded **3** eventually.



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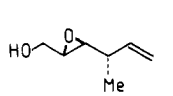

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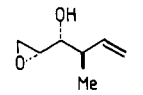

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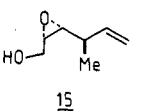

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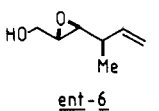

ent-6

The attempt to expand this sequence to **5a** met with limited success. Although **5e** could be obtained without difficulty, the ring closure with methoxide, regardless of the solvent, resulted in the formation of a 1:1 mixture of both epoxides **14** and **15**. The reason for the uncompleteness of the Payne rearrangement in this case may be seen in the fact that **15**, being a cis 2,3-epoxide, has a greatly reduced tendency of formation compared to the trans 2,3-isomer **13**. In fact, after inverting the 3-OH group of **14** under Mitsunobu conditions[15] and treating the resulting benzoate with methoxide in chloroform, the rearranged trans epoxide *ent*-**6**, identical in all spectral data with **6**, was obtained as the only product. The diastereomeric purity of **1**, **2**, and **3** was shown to be >95% by ^{13}C NMR. The optical purity may be assumed to be the same as that of the starting compounds **4a**/**5a** (>98%),[12] because

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the stereocenter at the methyl group has been left untouched throughout the synthesis.

1c and **2c** are of significant synthetic utility, as they are available in multigram quantities; for instance, 30 g of each isomer can routinely be prepared in about 1 week's time. Furthermore, the presence of the two synthetically equivalent but easily differentiable end groups allow chain elongations in either direction by straightforward aldehyde methodology. As an application, we embarked on the synthesis of appropriate erythronolide B fragments.[16] Our retrosynthetic analysis dissects the molecule into the fragments **16a** and **17a**, respectively, which could be combined by a Horner reaction. The central part of **16**, namely the stereocenters at C-10, 11, and 12, exactly correspond to those in 1 if the double-bond portion is considered as the precursor to the C-9-carbonyl in **16**; the remaining functionality may be attached to **1c** by standard procedures.[17] The right-hand fragment, **17a**, which is identical with the C(1)–C(7) section of erythronolide A as well, has been prepared from **2c** in the form of the methyl ester derivative **17b**. Specifically, **2c** was ozonized to aldehyde **18a**, which on Wittig reaction with [(α-carbomethoxyethoxy)ethylidene]triphenylphosphorane furnished the ester **18b** in an *E*/*Z* ratio of >97:3, in accordance with ample literature precedence.[18] No epimerization at C-4 could be detected. Osmylation with catalytic amounts of osmium tetraoxide converted **18b** into a 2:1 mixture of the diol esters **17b** and **19**, readily separable by HPLC in gram quantities. The configuration at the newly created stereocenters C-5 and C-6 was assigned by ^{13}C NMR. It is well-documented[19] that in stereotriplets of type **20**/**21** the central methyl group in **20**, where it is flanked by two syn, vic OR functions, absorbs about 5–6 ppm upfield with respect to the corresponding signal in **21** and typically falls into the region below 10 ppm, relative to Me_4Si. Indeed, the spectrum of **17b** shows signals at 8.37 (4-Me) and 12.12 (2-Me) ppm, whereas the signals of **19** appear at 13.42 and 13.98 ppm. Thus the postulated *all-syn*-3,4,5-OBnMeOH arrangement can only be present in **17b** and not in **19**.

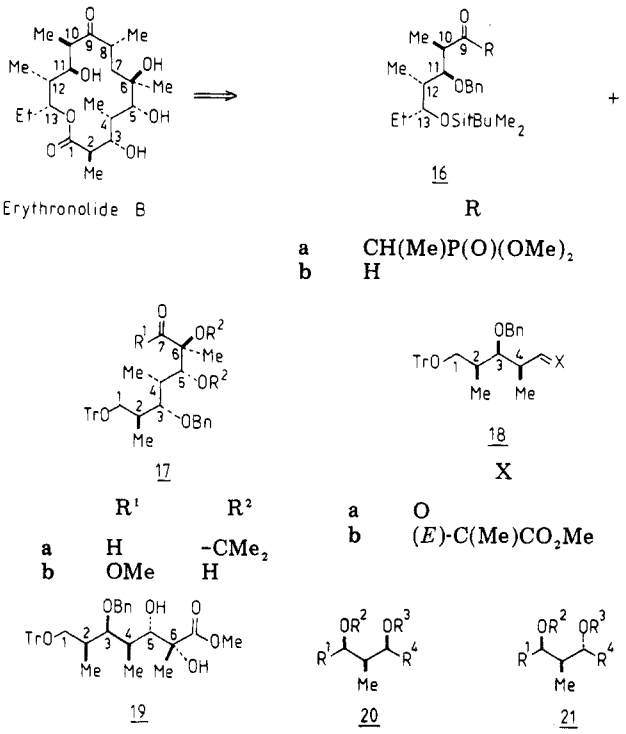
In conclusion, the basic macrolide synthons **1**, **2**, and **3** in unprotected and protected forms and the erythronolide B fragment **17b** have been prepared from (*R*)-2,3-*O*-isopropylideneglyceraldehyde by practical routes in gram quantities. Although the osmylation leading to **17b** proceeds with low stereocontrol, 2–3 g of homochiral material may be obtained in one series of experiments, taking less than 2 weeks. We thus feel in a good position to complete the synthesis of the macrolide aglycon in due course.

Experimental Section

Infrared spectra (IR) were obtained with a Perkin-Elmer IR 580B spectrometer. Nuclear magnetic resonance spectra (NMR) were recorded with a Bruker WH 270 or AC 250 spectrometer in $CDCl_3$ and are reported in ppm downfield of internal tetramethylsilane (δ units). Optical rotations were determined in $CHCl_3$ (unless stated otherwise) with a Perkin-Elmer 121 polarimeter at a wavelength of 589 nm at 20 °C. Mass spectra (MS) were recorded with a Varian MAT 711 spectrometer. HPLC separations were performed by using a Knauer pump with RI and UV detection. All reactions were performed in purified solvents and monitored by TLC plates (Merck 5554). Preparative column chromatography was performed on silica gel Merck 60, 230–400 mesh. (2*R*,3*S*,4*S*)- and (2*R*,3*R*,4*R*)-1,2-*O*-isopropylidene-4-methylhex-5-ene-1,2,3-triol (**4a** and **5a**) were prepared as described.[12]

(2*R*,3*S*,4*S*)- and (2*R*,3*R*,4*R*)-1,2-*O*-Isopropylidene-4-methyl-3-*O*-tosylhex-5-ene-1,2,3-triol (4b and 5b). **4a** (37.2 g, 200 mmol) and 4-(dimethylamino)pyridine (DAMP, 500 mg) were treated at 20 °C with a solution of tosyl chloride (freshly recrystallized from hexane, 40.0 g, 208 mmol) in pyridine (90 mL). After 2 days at room temperature, the mixture was concentrated under reduced pressure, diluted with water, and extracted with methylene chloride. The organic phase was washed with 2 N H_2SO_4 and water, dried ($MgSO_4$), and evaporated under reduced pressure to furnish 64 g of crude tosylate, which was purified by column chromatography (ethyl acetate/hexane, 1/10). **4b** (61.0 g, 90%) was obtained as a colorless oil, $[\alpha]^{20}_D$ +28.72° (*c* 1.99), which was used in the next step without further purification. IR (film): 2990, 1640, 1595, 1490, 1460, 1370, 1190, 1175, 1070, 920, 670 cm^{-1}. ^1H NMR: δ 1.01 (d, *J* = 6.75 Hz, 3 H, CH_3), 1.14 (s, 3 H, CH_3), 1.15 (s, 3 H, CH_3), 2.43 (s, 3 H, tosyl-CH_3), 2.70 (m, 1 H, 5-H); ABX system (δ_A 3.80, δ_B 3.90 J_{AB} = 10 Hz, $J_{AX} = J_{BX}$ = 7 Hz, 2 H, 1-H, 2-H), δ_X 4.10 (dt, *J* = 7 Hz, 1 H, 3-H), 4.70 (dd, $J_{4,3}$ = 2 Hz, $J_{4,5}$ = 7 Hz, 1 H, 4-H), 5.30 (m, 2 H, 7-H, 8-H), 5.70 (dq, 1 H, 6-H); AA'BB' system (δ_A 7.43, δ_B 7.80, $J_{AB} = J_{A'B'}$ = 8 Hz, 4 H, phenyl-H). Likewise 67.8 g (93%) of **5b** was obtained from **5a** (4.00 g, 205 mmol). ^1H NMR: 1.02 (d, *J* = 6.75 Hz, 3 H, CH_3), 1.25 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3), 2.43 (s, 3 H, CH_3, 2.67 (m, 1 H, 5-H); ABX system (δ_A 3.78, δ_B 3.89, J_{AB} = 10.0 Hz, J_{AX} = 7.5 Hz, J_{BX} = 5.0 Hz, 2 H, 1-H, 2-H); δ_X 4.0 (m, 1 H, 3-H), 4.68 (dd, $J_{4,3}$ = 5 Hz, $J_{4,5}$ = 7.5 Hz, 1 H, 4-H), 5.0 (m, 2 H, 7-H, 8-H), 5.70 (dq, 1 H, 6-H); AA'BB' system (δ_A 7.33, δ_B 7.78, $J_{AB} = J_{A'B'}$ = 8 Hz, 4 H, phenyl-H).

(2*R*,3*S*,4*S*)- and (2*R*,3*R*,4*R*)-4-Methyl-3-*O*-tosylhex-5-ene-1,2,3-triol (4c and 5c). **4b** (60.0 g, 176.3 mmol) in methanol (300 mL), water (40 mL), and trifluoroacetic acid (2 mL) was stirred at room temperature for 48 h. After evaporation of the solvent under reduced pressure, 50.1 g (94%) crude **4c** was obtained as a colorless oil ($[\alpha]^{20}_D$ +13.45° (*c* 2.25)), which was used in the next step without purification. ^1H NMR: δ 0.93 (d, *J* = 6.75 Hz, 3 H, CH_3), 2.48 (s, 3 H, tosyl-CH_3), 2.72 (m, 1 H, 5-H), 3.03 (m, 2 H, OH), 3.70 (m, 1 H, 3-H); ABX system (δ_A 3.76, δ_B



(17) In a preliminry study, intermediate **16b** was prepared from **1b** by (i) detritylation (CF_3CO_2H, CH_2Cl_2); (ii) oxidation (PCC, CH_2Cl_2); (iii) addition of EtMgBr in Et_2O; (iv) silylation (*t*-$BuMe_2SiCl$, imidazole, DMF); (v) ozonolysis (O_3, MeOH; then Me_2S) in 53% overall yield. The configuration at C-13 has not yet been secured. For a similar sequence, see: McGarvey, G. J.; Williams, J. M.; Hiner, R. N.; Matsubara, Y.; Oh, T. *J. Am. Chem. Soc.* **1986**, *108*, 4943.

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3.89, J_{AB} = 12 Hz, J_{AX} = 6 Hz, J_{BX} = 4 Hz, 2 H, 1-H, 2-H), δ_X 4.60 (dd, $J_{4,3}$ = 2 Hz, $J_{4,5}$ = 7 Hz, 1 H, 4-H), 5.00 (m, 2 H, 7-H, 8-H), 5.70 (dq, 1 H, 6-H), AA'BB' system (δ_A 7.40, δ_B 7.85, J_{AB} = $J_{A'B'}$ = 8 Hz, 4 H, phenyl). IR (film): 3450, 2990, 1640, 1600, 1500, 1460, 1360, 1175, 920, 670 cm^{-1}. Likewise, 54.2 g (94%) **5c** was obtained from **5b** (65.0 g, 191 mmol). ^{1}H NMR: 0.93 (d, J = 6.75 Hz, 3 H, CH_3), 2.49 (s, 3 H, CH_3), 2.57 (m, 2 H, OH), 2.73 (m, 1 H, 5-H), 3.74 (m, 1 H, 3-H); ABX system (δ_A 3.80, δ_B 3.90, J_{AB} = 12 Hz, J_{AX} = 5 Hz, J_{BX} = 3 Hz, 2 H, 1-H, 2-H), δ_X 4.51 (dd, $J_{4,3}$ = 3.4 Hz, $J_{4,5}$ = 8 Hz, 1 H, 4-H), 5.10 (m, 2 H, 7-H, 8-H); AA'BB' system (δ_A 7.46, δ_B 7.91, J_{AB} = $J_{A'B'}$ = 8 Hz, 4 H, phenyl-H).

(2*R*,3*S*,4*S*)- and (2*R*,3*R*,4*R*)-4-Methylhex-5-ene-1,2,3-triol (4d and 5d). **4a** (6.56 g, 35.3 mmol) in methanol (30 mL), water (10 mL), and trifluoroacetic acid (0.5 mL) was stirred at room temperature for 24 h and then evaporated to dryness under reduced pressure. The oily residue was dissolved in methylene chloride, washed with water, and dried ($MgSO_4$) to give **4d** (6.30 g, 97%) as colorless crystals of mp 68 °C. ^{1}H NMR: δ 1.00 (d, J = 7.5 Hz, 3 H, CH_3), 2.50 (m, 1 H, 5-H), 3.20 (m, 1 H, 3-H), 3.34 (m, 2 H, 1-H, 2-H), 3.60 (m, 1 H, 4-H), 4.08 (t, $J_{OH,1}$ = 5 Hz, $J_{OH,2}$ = 8 Hz, 1 H, OH), 4.16 (d, J = 5 Hz, 1 H, OH), 4.45 (d, J = 5 Hz, 1 H, OH); 5.00 (m, 2 H, 7-H, 8-H), 5.85 (m, 1 H, 6-H). Anal. Calcd for $C_7H_{14}O_3$: C, 57.52; H, 9.65. Found: C, 57.50; H, 9.41. Likewise, **5d** (6.90 g, 95%) was obtained on hydrolysis of **5a** (7.34 g, 39.5 mmol). ^{1}H NMR: δ 1.08 (d, J = 7.5 Hz, 3 H, CH_3), 2.50 (m, 1 H, 5-H), 2.75 (d, J = 5 Hz, 1 H, oH), 3.30 (m, 2 H, 1-H, 2-H), 3.60 (m, 1 H, 4-H), 3.70 (m, 1 H, 3-H), 3.80 (m, 2 H, OH), 5.20 (m, 2 H, 7-H, 8-H), 5.90 (dq, 1 H, 6-H).

(2*R*,3*R*,4*S*)- and (2*R*,3*S*,4*R*)-Epoxy-4-methylhex-5-en-1-ol (6 and 7). **4c** (40.0 g, 133 mmol) in dichloromethane (120 mL) was treated with a solution of 7.0 g of sodium (7.0 g, 300 mL) in methanol (160 mL) for 30 min at 22 °C. The mixture was diluted with water, and the organic phase was separated, washed with water, dried ($MgSO_4$), evaporated, and distilled to furnish **6** (11.20 g, 70%) as a colorless oil with bp 70 °C/0.01 mm and $[\alpha]^{20}_D$ +7.77° (*c* 1.35, methanol), 1.27 (*c* 2.21). IR (film): 3450, 2990, 1640, 1050, 920 cm^{-1}. ^{1}H NMR: δ 1.15 (d, J = 6.75 Hz, 3 H, CH_3), 2.15 (m, 1 H, 3-H), 2.24 (m, 1 H, OH), 2.84 (dd, $J_{4,3}$ = 2 Hz, $J_{4,5}$ = 7 Hz, 1 H, 4-H), 3.00 (dt, $J_{3,1}$ = 4 Hz, $J_{3,2}$ = 2 Hz, $J_{3,4}$ = 2 Hz, 1 H, 3-H); AB part of an ABX system (δ_A 3.62, δ_B 3.93, J_{AB} = 12 Hz, J_{AX} = 4 Hz, J_{BX} = 2 Hz, 2 H, 1-H, 2-H), 5.10 (m, 2 H, 7-H, 8-H), 5.80 (dq, 1 H, 6-H). ^{13}C NMR ($CDCl_3$): δ 15.77 (C-7), 38.76 (C-4), 57.55 (C-1), 59.08 (C-3), 61.54 (C-2), 114.77 (C-6), 138.33 (C-5). Anal. Calcd for $C_7H_{12}O_2$: C, 65.64; H, 9.44. Found: C, 65.26; H, 9.43. Likewise, **7** (13.75 g, 64%) was obtained from **5c** (50.0 g, 166 mmol) as a colorless oil of bp 90 °C/0.03 mm and $[\alpha]^{20}_D$ +54.92° (*c*, 5.49). ^{1}H NMR: δ 1.20 (d, J = 6.75 Hz, 3 H, CH_3), 2.10 (m, 1 H, 5-H), 2.84 (dd, $J_{4,3}$ = 4.0 Hz, $J_{4,5}$ = 9.45 Hz, 1 H, 4-H), 3.24 (dt, $J_{3,1}$ = 6.75 Hz, $J_{3,2}$ = 5.4 Hz, $J_{3,4}$ = 4.0 Hz, 1 H, 3-H); AB part of ABX system (δ_A 3.70, δ_B 3.90, J_{AB} = 10.8, J_{AX} = 6.75 Hz, J_{BX} = 4.0 Hz, 2 H, 1-H, 2-H), 4.90 (m, 2 H, 7-H, 8-H), 5.76 (dq, 1 H, 6-H).

(2*R*,3*S*,4*S*)-4-Methyl-1-*O*-tosylhex-5-ene-1,2,3-triol (4e and 5e). **4d** (5.80g, 39.7 mmol) was treated with tosyl chloride (7.00 g, 36.8 mmol) in pyridine (15 mL) at −30 °C for 1 h. The mixture was diluted with water and extracted with methylene chloride. The organic phase was washed with water, dried ($MgSO_4$), and evaporated to furnish **4e** (6.3 g, 53%) as colorless crystals of mp 60–61 °C. ^{1}H NMR: δ 1.06 (d, J = 6.75 Hz, 3 H, CH_3), 2.00 (d, J = 5 Hz, 1 H, OH), 2.44 (s, 3 H, OCH_3), 2.52 (m, 1 H, 5-H), 2.56 (d, J = 5 Hz, 1 H, OH), 3.46 (dd, $J_{4,3}$ = 5 Hz, $J_{4,5}$ = 10 Hz, 1 H, 4-H), 3.80 (m, 1 H, 3-H); AB part of ABX system (δ_A 4.12, δ_B 4.30, J_{AB} = 10 Hz, J_{AX} = 5 Hz, J_{BX} = 4 Hz, 2 H, 1-H, 2-H), 5.10 (m, 2 H, 7-H, 8-H), 5.75 (m, 1 H, 6-H); AA'BB' system (δ_A 7.35, δ_B 7.80, J_{AB} = $J_{A'B'}$ = 8 Hz). Anal. Calcd for $C_{14}H_{20}O_5S$: C, 55.99; H, 6.71; S, 10.67. Found: C, 55.80; H, 6.93; S, 10.67. Likewise, **5d** (5.50 g, 37.7 mmol) was converted into **5e** (7.89 g, 70%), colorless crystals of mp 64–65 °C. ^{1}H NMR: δ 1.04 (d, J = 6.75 Hz, 3 H, CH_3), 2.35 (m, 1 H, 5-H), 2.56 (m, 2 H, OH), 3.34 (dd, $J_{4,3}$ = 2 Hz, $J_{4,5}$ = 6Hz, 1 H, 4-H), 3.86 (dt, $J_{3,1}$ = 2 Hz, $J_{3,2}$ = 4 Hz, $J_{3,4}$ = 2 Hz, 1 H, 3-H); AB part of ABX system (δ_A, = δ_B = 4.08, J_{AB} = 4 Hz, J_{AX} = 2 Hz, J_{BX} = 4 Hz, 2 H, 1-H, 2-H), 5.8 (m, 2 H, 7-H, 8-H), 5.76 (dq, 1 H, 6-H); AA'BB' system (δ_A 7.36, δ_B 7.80, J_{AB} = $J_{A'B'}$ = 8 Hz, 4 H, Ar H). Anal. Calcd for $C_{14}H_{20}O_5S$: C, 55.99; H, 6.71; S, 10.67. Found: C, 55.42; H, 6.69; S, 10.97. ^{13}C NMR: δ 16–78 (C-7, CH_3), 35.80 (C-4), 57.17 (C-1), 59.83 (C-3), 59.86 (C-2), 114.20 (C-6), 138.05 (C-5). Anal. Calcd for $C_7H_{12}O_2$: C, 65.67; H, 9.44. Found: C, 65.12; H, 9.56.

(2*S*,3*R*,4*S*)- and (2*S*,3*S*,4*R*)-2,4-Dimethylhex-5-ene-1,3-diol (1a and 2a). Cuprous cyanide (24.3 g, 272 mmol) in ether (110 mL) was treated dropwise under vigorous stirring with methyllithium (1.6 M in ether, 346 mL, 554 mmol) at 78 °C. After adding **6** (10.0 g, 69.3 mmol) dropwise from a canula, cooling was discontinued and the greyish mixture was stirred for 15 h. Then a solution of ammonium chloride in concentrated ammonia was added, and the organic layer was separated, washed with water, dried ($MgSO_4$), and evaporated to give a yellow oil, which was purified by chromatography (hexane/ethyl acetate, 3/1) to give **1a** (8.18 g, 80%) as a colorless oil. $[\alpha]^{20}_D$ −11.31° (*c* 2.13). IR (film): 3350, 2990, 1640, 1460, 1030, 1000, 970, 910 cm^{-1}. ^{1}H NMR: δ 0.90 (d, J = 6.75 Hz, 3 H, CH_3), 1.04 (d, J = 6.75 Hz, 3 H, CH_3), 1.80 (m, 1 H, 3-H), 2.50 (m, 1 H, 5-H), 2.70 (m, 1 H, OH), 3.40 (m, 1 H, OH), 3.50 (dd, $J_{4,3}$ = 4 Hz, $J_{4,5}$ = 8 Hz, 1 H, 4-H); ABX system (δ_A 3.60, δ_B 3.80, J_{AB} = 11 Hz, J_{AX} = 8 Hz, J_{BX} = 4 Hz, 2 H, 1-H, 2-H), 5.00 (m, 2 H, 7-H, 8-H), 5.90 (dq, 1 H, 6-H). ^{13}C NMR: δ 11.85 (C-8), 13.84 (C-7), 36.92 (C-2), 40.20 (C-4), 67.74 (C-1), 79.58 (C-3), 115.17 (C-6), 141.55 (C-5). Anal. Calcd for $C_8H_{16}O_2$: C, 66.64; H, 11.18. Found: C, 66.69; H, 11.46. Likewise, **2a** (7.16 g, 71%) was obtained from **8** (10.0 g, 69.3 mmol), colorless crystals with mp 81–82 °C (hexane), $[\alpha]^{20}_D$ +40.1° (*c*, 3.2). ^{1}H NMR: δ 0.94 (d, J = 6.75 Hz, 3 H, CH_3), 1.13 (d, J, = 6.75 Hz, 3 H, CH_3), 1.80 (m, 1 H, 3-H), 2.30 (m, 1 H, 5-H), 3.10 (m, 1 H, OH), 3.20 (m, 1 H, OH), 3.58 (dd, $J_{4,3}$ = 2 Hz, $J_{4,5}$ = 9.5 Hz, 1 H 4-H); AB part of ABX system (δ_A = δ_B = 3.70, 2 H, 1-H, 2-H), 5.00 (m, 2 H, 7-H, 8-H), 5.60 (dq, 1 H, 6-H). ^{13}C NMR: δ 8.91 (C-8), 17.16 (C-7), 36.61 (C-2), 42.15 (C-4), 67.51 (C-1), 76.49 (C-3), 114.65 (C-6), 140.83 (C-5). Anal. Calcd for $C_8H_{16}O_2$: C, 66.64; H, 11.18. Found: C, 66.51; H, 11.23.

(2*S*,3*R*,4*S*)- and (2*S*,3*S*,4*R*)-2,4-Dimethyl-1-*O*-tritylhex-5-ene-1,3-diol (1b and 2b). **1a** (7.00 g, 48.65 mmol) in pyridine (100 mL) was treated with trityl chloride (16.22 g, 58.33 mmol) and a catalytic amount of DMAP for 5 h at 22 °C. The mixture was poured on ice and extracted with methylene chloride. The organic layer was washed, dried ($MgSO_4$), and evaporated. The oily residue was purified by chromatography (hexane/ethyl acetate, 6/1) to give **1b** (16.33 g, 87%) as a colorless oil, $[\alpha]^{20}_D$ −10.13° (*c*, 3.85). IR (film): 3500, 2960, 1640, 1600, 1490, 1440, 1230, 1160, 1070, 710 cm^{-1}. ^{1}H NMR: δ 0.98 (d, J = 6.75 Hz, 3 H, CH_3), 1.02 (d, J = 6.75 Hz, 3 H, CH_3), 1.85 (m, 2 H, 5-H), 2.05 (m, 1 H, 3-H), 3.10 (m, 1 H, OH); AB part of ABX system (δ_A 3.2/, δ_B 3.28, J_{AB} = 8 Hz, J_{AX} = 5 Hz, J_{BX} = 4 Hz, 2 H, 1-H, 2-H), 3.30 (m, 1 H, 4-H), 4.80 (m, 2 H, 7-H, 8-H), 5.70 (dq, 1 H, 6-H), 7.30 (m, 10 H, trityl-H), 7.40 (m, 5 H, trityl-H). Anal. Calcd for $C_{27}H_{30}O_2$: C, 83.90; H, 7.82. Found: C, 83.60; H, 7.53. Likewise, **2a** (7.00 g, 48.65 mmol) was converted into **2b** (17.46 g, 93%) $[\alpha]^{20}_D$ −17.9° (*c* 1). ^{1}H NMR: δ 1.03 (d, J = 6.75 Hz, 3 H, CH_3), 1.06 (d, J = 6.75 Hz, 3 H, CH_3), 1.90 (m, 1 H, 3-H), 2.25 (m, 1 H, 5-H), 2.56 (d, J = 3.0 Hz, 1 H, OH); AB part of ABX system (δ_A 3.10, δ_B 3.22, J_{AB} = 9.5 Hz, J_{AX} = 4 Hz, J_{BX} = 5 Hz, 2 H, 1-H, 2-H), 3.45 (dd, $J_{4,3}$ = 2 Hz, $J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 5.00 (m, 2 H, 7-H, 8-H), 5.60 (dq, 1 H, 6-H), 7.20 (m, 10 H, Ar H); 7.40 (m, 5 H, Ar H). Anal. Calcd for $C_{27}H_{30}O_2$: C, 83.90; H, 7.82. Found: C, 83.92; H, 7.78.

(2*S*,3*R*,4*S*)- and (2*S*,3*S*,4*R*)-3-*O*-Benzyl-2,4-dimethyl-1-*O*-tritylhex-5-ene-1,3-diol (1c and 2c). Sodium hydride (2.33 g, 47.5 mmol), as a 50% suspension in mineral oil, was washed with hexane, dried by suction, and suspended in DMF (230 mL). Then **1b** (15.00 g, 38.8 mmol) in DMF (78 mL) and benzyl chloride (5.12 g, 40.3 mmol) were added successively at 22 °C and the mixture was stirred at 50 °C for 22 h, concentrated under reduced pressure, filtrated, and extracted with methylene chloride. The organic phase was washed, dried ($MgSO_4$), and evaporated to give a yellow oil, which was purified by chromatography (hexane/ethyl acetate, 10/1) to give **1c** (15.84 g, 86%) as a colorless oil, $[\alpha]^{20}_D$ +2.46° (*c* 3.3). ^{1}H NMR: δ 1.00 (d, J = 7.0 Hz, 3 H, CH_3), 1.08 (d, J = 6.7 Hz, 3 H, CH_3), 2.06 (m, 1 H, 2-H), 2.36 (m, 1 H, 4-H), 3.18 (dd, J = 6.7 and 9.4 Hz, 1 H, 3-H), 3.28 (m, 2 H, 1-H), 4.08 (d, J = 12.1 Hz, 1 H, CH_2Ph), 4.48 (d, J = 12.1 Hz, 1 H, CH_2Ph), 4.88 (d, J = 11 Hz, 1 H, 6-H), 4.94 (d, J = 18 Hz, 1 H, 6-H), 5.74 (ddd, J = 11 and 18 and 7.5 Hz, 1 H, 5-H), 6.9–7.6 (m, 20 H). ^{13}C NMR: 14.61, 15.28, 37.27, 40.30, 65.11, 65.76, 74.29, 85.03, 113.74, 126.76, 126.86, 126.98, 127.03, 127.14, 127.46, 127.60, 127.70,

127.79, 128.04, 128.20, 128.72, 128.79, 128.85, 142.56, 144.15, 144.42. Likewise, **2c** (17.56 g, 90%) was obtained from **2b** (15.00 g, 38.8 mmol), $[\alpha]^{20}_D$ +15.1° (*c* 1). ^{1}H NMR: δ 0.84 (d, *J* = 6.5 Hz, 3 H, CH_3), 1.08 (d, *J* = 6.5 Hz, 3 H, CH_3), 2.07 (m, 1 H, 2-H), 2.40 (m, 1 H, 4-H); AB part of ABX system: δ_A 3.03, δ_B 3.11, J_{AB} = 8.6 Hz, J_{AX} = 7.8 Hz, J_{BX} = 5.5 Hz, 2 H, 1-H), 3.52 (dd, *J* = 2,5 Hz, *J* = 8.0 Hz, 1 H, 3-H); AB system (δ_A 4.30, δ_B 4.43, J_{AB} = 11 Hz, 2 H, OCH_2Ph), 5.01 (d, *J* = 10.5 Hz, 1 H, 6-H), 5.06 (d, *J* = 16.7 Hz, 1 H, 6-H), 5.81 (ddd, *J* = 10.5 Hz, *J* = 16.7 Hz, *J* = 7.8 Hz, 1 H, 5-H), 7.08 (m, 2 H, Ar H), 7.26 (m, 13 H, Ar H), 7.44 (m, 5 H, Ar H). ^{13}C NMR: δ 11.18, 17.08, 36.65, 41.49, 66.36 (C-1), 74.74, 83.21 (C-3), 113.99, 126.90, 127.22, 127.64, 127.73, 128.10, 128.75, 142.02, 144.39. Anal. Calcd for $C_{34}H_{36}O_2$: C, 85.67; H, 7.62. Found: C, 85.87; H, 8.20.

(2*S*,4*S*)- and (2*S*,3*r*,4*R*)-2,4-Dimethyl-1,3,5-tri-*O*-acetylpentane-1,3,5-triol (8 and 9). **1a** (950 mg, 6.60 mmol) and a catalytic amount of DMAP in pyridine (5 mL) were treated with acetic anhydride (700 mg, 6.86 mmol) for 14 h at 22 °C. Hydrolytic workup furnished a quantitative yield of the crude diacetate, which was ozonized in methanol (10 mL) at −78 °C followed by reductive workup with sodium borohydride (960 mg) at 0 °C. The solvent was evaporated under reduced pressure and the crude alcohol was treated with acetic anhydride as described above to give **8** (420 mg, 60%) as a colorless oil, $[\alpha]^{20}_D$ −3.19° (*c*, 1.63). ^{1}H NMR: δ 0.88 (d, *J* = 6.75 Hz, 3 H, CH_3), 0.99 (d, *J* = 6.75 Hz, 3 H, CH_3), 2.05 (s, 3 H, CH_3), 2.07 (s, 3 H, CH_3), 2.20 (m, 2 H, 3-H, 5-H, 3.80–4.40 (m, 4 H, 1,2,6,7-H), 4.99 (dd, $J_{4,3}$ = 4 Hz, $J_{4,5}$ = 8.1 Hz, 1 H, 4-H). ^{13}C NMR: δ 10.52–14.20 (C-6, C-7), 20.63 (2 × CH_3, OAc), 20.73 (1 × CH_3, OAc), 33.38, 33.83 (C-2, C-4), 66.11 and 65.76 (C-1, C-5), 73.95 (C-3), 170.29 (1 × C=O), 170.85 (2 × C=O). MS: *m/e* calcd for ($M^+ - C_5H_9O_2$) 173.08138. Found: 173.08141. Likewise, **9** (400 mg, 57%) was obtained from the degradation of **2a** (960 mg, 6.60 mmol), $[\alpha]^{20}_D$ < −0.09° (*c* 2.05). ^{1}H NMR: δ 0.96 (d, *J* = 6.75 Hz, 6 H, 2 × CH_3), 2.07 (s, 6 H, 2 × CH_3), 2.08 (s, 3 H, CH_3), 2.12 (m, 2 H, 2-H, 4-H); AB part of ABX system (δ_A 3.92, δ_B 4.08, J_{AB} = 10.8 Hz, J_{AX} = J_{BX} = 5.4 Hz, 4 H, 1-H, 5-H), 5.04 (dd, $J_{4,3}$ = 5.4 Hz, $J_{4,5}$ = 8.1 Hz, 1 H, 3-H). ^{13}C NMR: δ 12.02 (C-6 and C-7), 20.61 (2 × CH_3 from OAc), 20.70 (CH_3 from OAc), 34.25 (C-2 and C-4), 65.96 (C-1 and C-5), 73.46 (C-3), 170.36 (C=O), 170.78 (2 × C=O). Anal. Calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08. Found: C, 56.76; H, 8.54.

Mitsunobu Inversion of 1b/2b: (2*S*,3*S*,4*S*)- and (2*S*,3*R*,4*R*)-2,4-Dimethyl-3-*O*-(*p*-nitrobenzoyl)-1-*O*-trityl-hex-5-ene-1,3-diol (10 and 11). **1b** (560 mg, 1.46 mmol), *p*-nitrobenzoic acid (334 mg, 2.00 mmol), and triphenylphosphine (524 mg, 2.00 mmol) in THF (10 mL) were treated dropwise with diethyl azodicarboxylate (348 mg, 2.00 mmol). The mixture was stirred at 22 °C for 120 h. Chromatographic workup (ethyl acetate/hexane, 3/1) furnished **10** (395 mg, 50%) as a colorless oil. ^{1}H NMR: δ 1.00 (d, *J* = 6.75 Hz, 3 H, CH_3), 1.12 (d, *J* = 6.75 Hz, 3 H, CH_3), 2.30 (m, 1 H, 3-H), 2.60 (m, 1 H, 5-H); AB part of ABX system (δ_A 3.04, δ_B 3.24, J_{AB} = 10 Hz, J_{AX} = 7.5 Hz, J_{BX} = 5 Hz, 2 H, 1-H, 2-H), 5.00 (m, 2 H, 7-H, 8-H), 5.16 (dd, $J_{4,3}$ = 5 Hz, $J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 5.72 (dq, 1 H, 6-H), 7.30 (m, 15 H, trityl-H); AA′BB′ system (δ_A 7.94, δ_B 8.20, J_{AB} = $J_{A'B'}$ = 8 Hz, 4 H, Ar H). MS: *m/e* calcd for M^+, 535.23587. Found: 535.23510. Likewise, **11** (314 mg, 45%) was obtained from **2b** (500 mg, 1.30 mmol). ^{1}H NMR: δ 1.00 (d, *J* = 6.75 Hz, 3 H, CH_3), 1.02 (d, *J* = 6.75 Hz, 3 H, CH_3), 2.22 (m, 1 H, 3-H), 2.56 (m, 1 H, 5-H); AB part of ABX system (δ_A 3.09, δ_B 3.24, J_{AB} = 9.5 Hz, J_{AX} = 5 Hz, J_{BX} = 3 Hz, 2 H, 1-H, 2-H), 5.08 (m, 2 H, 7-H, 8-H), 5.36 (dd, $J_{4,3}$ = 5 Hz, $J_{4,5}$ = 8.5 Hz, 1 H, 4-H), 5.76 (dq, 1 H, 6-H), 7.30 (m, 15 H, Ar H); AA′BB′ system (δ_A 8.08, δ_B 8.30, J_{AB} = $J_{A'B'}$ = 8 Hz, 4 H, *p*-nitrobenzoyl-H). MS: *m/e* calcd for M^+, 535.23587. Found: 535.2396.

(2*R*,3*S*,4*S*)-1,2-Epoxy-4-methylhex-5-en-3-ol (12). **4e** (6.00 g, 20.0 mmol) in methanol (10 mL) was treated with a solution of sodium (500 mg, 21.7 mmol) in methanol (5 mL) at 4 °C for 10 min. Then water was added and the mixture was extracted with methylene chloride. The organic phase was washed, dried ($MgSO_4$), and evaporated. The oily residue was purified by chromatography (ethyl acetate/hexane, 3/1) to furnish **12** (1.20 g, 43%) as a colorless oil, $[\alpha]^{20}_D$ +9.62° (*c* 0.53). ^{1}H NMR: δ 1.16 (d, *J* = 6.75 Hz, 3 H, CH_3), 1.80 (d, *J* = 5 Hz, 1 H, OH), 2.50 (m, 1 H, 5-H); ABX system (δ_A 2.74, δ_B 2.84, J_{AB} = 8 Hz, J_{AX} = J_{BX} = 3 Hz, 2 H, 1-H, 2-H), 3.00 (m, 1 H, 3-H), 3.60 (m, 1 H, 4-H), 5.10 (m, 2 H, 7-H, 8-H), 5.85 (m, 1 H, 6-H). ^{13}C NMR: δ 15.60 (C-7), 42.14 (C-4), 43.89 (C-2), 53.05 (C-1), 72.23 (C-3), 115.65 (C-6), 139.30 (C-6), 139.30 (C-5). Anal. Calcd for $C_7H_{12}O_2$: C, 65.64; H, 9.38.

(2*S*,3*S*,4*S*)-2,3-Epoxy-4-methylhex-5-en-1-ol (13). **4e** (1.77 g, 5.90 mmol) in methylene chloride (20 mL) was treated with a solution of sodium (1.5 g) in methanol (15 mL) at 22 °C. After 15 min water was added and the mixture was worked up as described for the preparation of **12**. **13** (600 mg, 80%) was obtained as a colorless oil after distillation at 55 °C/0.03 mm, $[\alpha]^{20}_D$ −45.08° (*c* 0.61). ^{1}H NMR: δ 1.08 (d, *J* = 6.75, 3 H, CH_3), 2.22 (m, 1 H, 5-H), 2.88 (dd, $J_{4,3}$ = 3 Hz, $J_{4,5}$ = 8 Hz, 1 H, 4-H), 3.00 (m, 1 H, 3-H), 3.00 (m, 1 H, OH); ABX system (δ_A 3.60, δ_B 3.88, J_{AB} = 13 Hz, J_{AX} = 7 Hz, J_{BX} = 4 Hz, 2 H, 1-H, 2-H), 5.00 (m, 2 H, 7-H, 8-H), 5.77 (dq, 1 H, 6-H). ^{13}C NMR: δ 15.78 (C-7), 38.86 (C-4), 57.00 (C-1), 59.14 (C-3), 61.74 (C-2), 115.17 (C-6), 139.23 (C-5). Anal. Calcd for $C_7H_{12}O_2$: C, 65.60; H, 9.44. Found: C, 64.80; H, 9.34.

(2*R*,3*S*,4*S*)-2,4-Dimethylhex-5-ene-1,3-diol (3). The cuprate ring opening of **13** (2.00 g, 15.62 mmol) was performed in analogy to the preparation of **1a/2a**. **3** (1.02 g, 43%) was obtained as a colorless oil, $[\alpha]^{20}_D$ −23.63° (*c* 0.44). ^{1}H NMR: δ 0.96 (d, *J* = 6.75 Hz, 3 H, CH_3), 1.11 (d, *J* = 6.75 Hz, 3 H, CH_3), 1.82 (m, 1 H, 3-H), 2.44 (m, 1 H, 5-H), 2.44 (m, 1 H, OH), 2.75 (m, 1 H, OH), 3.40 (dd, $J_{4,3}$ = 5 Hz, $J_{4,5}$ = 7.5 Hz, 1 H, 4-H); AB part of ABX system (δ_A 3.64, δ_B 3.80, J_{AB} = 11.25 Hz, J_{AX} = 6.25 Hz, J_{BX} = 2.5 Hz, 2 H, 1-H, 2-H), 5.10 (m, 2 H, 7-H, 8-H), 5.84 (dq, 1 H, 6-H). ^{13}C NMR: δ 14.02 (C-8), 17.05 (C-7), 37.27 (C-2), 41.15 (C-4), 67.32 (C-3), 80.39 (C-1), 116.41 (C-6), 139.13 (C-5). MS: *m/e* calcd for $M^+ - H_2O$, 126.10447. Found: 126.10411.

(2*R*,3*R*,4*R*)-1,2-Epoxy-4-methylhex-5-en-3-ol (14). The compound was prepared from **5e** (6.00 g, 20.0 mmol) as described for **4e**. **14** (1.40 g, 50) was obtained as a colorless oil, $[\alpha]^{20}_D$ +20.21 (*c* 0.48). ^{1}H NMR: δ 1.16 (d, *J* = 6.75 Hz, 3 H, CH_3), 2.00 (d, *J* = 5.4 Hz, 1 H, OH), 2.50 (m, 1 H, 5-H); AB part of ABX system (δ_A 2.74, δ_B 2.84, J_{AB} = 5.4 Hz, J_{AX} = 2.7 Hz, J_{BX} = 4.0 Hz, 2 H, 1-H, 2-H), 3.08 (dt, $J_{3,1}$ = 2.7 Hz, $J_{3,2}$ = 4.0 Hz, $J_{3,4}$ = 5.4 Hz, 1 H, 3-H), 3.36 (dd, $J_{4,3}$ = 5.4 Hz, $J_{4,5}$ = 10.8 Hz, 1 H, 4-H), 5.16 (m, 2 H, 7-H, 8-H), 5.88 (dq, 1 H, 6-H). ^{13}C NMR: δ 15.57 (C-7), 42.45 (C-1), 44.88 (C-2), 53,51 (C-4), 74.24 (C-3), 116.14 (C-6), 139.49 (C-5). Anal. Calcd for $C_7H_{12}O_2$: C, 65.64; H, 944. Found: C, 65.23; H, 9.34.

(2*S*,3*R*,4*R*)-2,3-Epoxy-4-methylhex-5-en-1-ol (15). **5e** (6.00 g, 20.0 mmol) was treated with sodium methoxide as described in the preparation of **6**. A mixture (2.10 g, 75%) of **14** and **15** was obtained in a ratio of about 1:1. On chromatography (ethyl acetate/hexane, 3/1) **14** and **15** were quantitatively separated. Analytical data of **15**: $[\alpha]^{20}_D$ +56.25° (*c* 0.16). ^{1}H NMR: δ 1.12 (d, *J* = 6.74 Hz, 3 H, CH_3), 2.04 (m, 1 H, OH), 2.14 (m, 1 H, 5-H), 2.88 (dd, $J_{4,3}$ = 4 Hz, $J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 3.24 (dt, $J_{3,1}$ = 4 Hz, $J_{3,2}$ = 6.8 Hz, $J_{3,4}$ = 4 Hz, 1 H, 3-H); AB part of ABX system (δ_A 3.76, δ_B 3.88, J_{AB} = 12.2 Hz, J_{AX} = 4 Hz, J_{BX} = 6.8 Hz, 2 H, 1-H, 2-H), 5.16 (m, 2 H, 7-H, 8-H), 5.92 (dq, 1 H, 6-H). ^{13}C NMR: δ 16.18 (C-7), 36.41 (C-4), 56.78 (C-1), 60.75 (C-3), 60.90 (C-2), 114.79 (C-6), 140.13 (C-5). Anal. Calcd for $C_7H_{12}O_2$: C, 65.64; H, 9.44. Found: C, 65.43; H, 9.66.

Mitsunobu Reaction of 14 and Subsequent Payne Rearrangement: (2*S*,3*S*,4*R*)-2,3-Epoxy-4-methylhex-5-en-1-ol (*ent*-6). **14** (500 mg, 3.90 mmol), benzoic acid (500 mg, 4.10 mmol), and triphenylphosphine (1.20 g, 4.85 mmol) in THF (20 mL) were treated dropwise with ethyl azodicarboxylate (700 mg, 7.10 mmol) in THF (5 mL) at 22 °C. After an additional 14 h the solvent was evaporated under reduced pressure and the oily residue was treated with methanolate in methylene chloride as described for the preparation of **6**. *ent*-**6** (320 mg, 64%) was isolated by chromatography as a colorless oil, whose ^{1}H and ^{13}C NMR spectra were identical with those of **6**.

(2*S*,3*R*,4*S*)-3-(Benzyloxy)-2,4-dimethyl-5-(trityloxy)pentanal (18a). **2c** (15.00 g, 31.45 mmol) in methanol (500 mL) was ozonized at −78 °C until a slightly blue solution resulted. Excess ozone was removed by bubbling oxygen through the mixture and dimethyl sulfide (19.50 g, 314.5 mmol) was added. After 30 min the solvent was evaporated under reduced pressure and the oily residue was purified by chromatography (hexane/ethyl acetate, 10/1) to give **18a** (9.75 g, 67%) as a colorless oil, $[\alpha]^{20}_D$ +16.6° (*c* 5). ^{1}H NMR: δ 1.00 (d, *J* = 7 Hz, 3H $-CH_3$); 1.08 (d, *J* = 7

Hz, $-CH_3$); 1.99 (m, 1 H, H-4); 2.48 (m, 1 H, H-2); AB-part of ABX-system (δ_A 3.07, δ_B 3.12, J_{AB} = 9 Hz, J_{AX} = 5.5 Hz, J_{BX} = 6.8 Hz, 2 H, H-5); 4.04 (t, $J_{3,2} = J_{3,4}$ = 5.5 Hz, 1 H, H-3); AB-system (δ_A 4.31, δ_B 4.43, J_{AB} = 11 Hz, 2 h, OCH_2Ph), 7.19 (m, 15 H, phenyl-H), 7.47 (m, 5 H, phenyl-H), 9.74 (d, J = 1.9 Hz, CHO). ^{13}C NMR: δ 11.18 and 17.08 (2-CH_3 and 4-CH_3); 36.65 (C-4); 41.49 (C-2); 66.36 (C-5); 74.74 (-OCH_2-Ph); 83.21 (C-3); 126.90, 127.22, 127.64, 127.73, 128.10, 128.75 and 144.39 (20C, phenyl-C); 142.02 (C-1). Anal. Calcd for $C_{33}H_{34}O_3$: C, 82.64; H, 7.14. Found: C, 82.60; H, 7.31.

(4*R*,5*R*,6*S*)-Methyl 5-(Benzyloxy)-2,4,6-trimethyl-7-(trityloxy)-(*E*)-hept-2-enoate (18b). **18a** (8.40 g, 18.16 mmol) in THF (80 mL) was treated with (α-carbomethoxyethylidene)triphenylphosphorane (6.96 g, 20.0 mmol) for 24 h at 22 °C. After removal of the solvent the crude product was chromatographed (hexane/ethyl acetate, 10/1) to furnish **18b** (5.20 g, 52%) as a colorless oil, $[\alpha]^{20}_D$ +11.6° (c 2). IR (film): 3500, 3030, 3060, 2950, 1730, 1640, 1590, 1490, 1250, 1060, 910, 730, 700 cm^{-1}. ^1H NMR: δ 0.86 (d, J = 7.5 Hz, 3 H, 6-CH_3), 1.12 (d, J = 7.5 Hz, 3 H, 4-CH_3), 1.85 (s, 2 H, 2-CH_3), 1.94 (m, 1 H, H-6), 2.76 (m, 1 H, H-4); AB part of ABX system (δ_A 3.08, δ_B 3.14, J_{AB} = 9.2 Hz, J_{AX} = 8.0 Hz, J_{BX} = 6.0 Hz, 2 H, H-7), 3.61 (dd, J = 2.7 Hz, J = 8.5 Hz, 1 H, H-5), 3.74 (s, 3 H, OCH_3); AB system (δ_A 4.33, δ_B 4.44, J_{AB} = 11.0 Hz, 2 H, OCH_2Ph), 6.6 (dd, J = 10.7 Hz, J = 1.6 Hz, 1 H, H-3), 7.10 (m, 2 H, phenyl-H), 7.22 (m, 13 H, phenyl-H), 7.44 (m, 5 H, phenyl-H). ^{13}C NMR: δ 11.20 and 12.47 (6- and 2-CH_3), 16.66 (4-CH_3), 37.09 and 37.37 (C-4 and C-6), 51.59 (OCH_3), 66.17 (C-7), 74.99 (OCH_2Ph), 82.98 (C-5), 86.57 (4-CH_3), 126.85–128.51, 138.60 and 144.15 (20 phenyl-C, C-3 and C-2), 168.80 (C-1). Anal. Calcd for $C_{37}H_{40}O_4$: C, 80.99; H, 7.35. Found: C, 80.88; H, 7.59.

(2*S*,3*R*,4*R*,5*R*,6*S*)- and (2*R*,3*S*,4*R*,5*R*,6*S*)-Methyl 5-(Benzyloxy)-2,3-dihydroxy-2,4,6-trimethyl-7-(trityloxy)-heptanoate (17b and 19). **18b** (5.00 g, 9.13 mmol) was added dropwise to *N*-methylmorpholine *N*-oxide hydrate (2.08 g, 13.54 mmol) and osmium tetraoxide (0.83 mL of a 1% solution in *tert*-butyl alcohol) dissolved in a mixture of water (5 mL) and acetone (2.1 mL). After 18 h at 22 °C, a suspension of sodium hydrogen sulfite (0.5 g), magnesium silicate (4 g), and water (50 mL) was added, and the mixture was stirred for another 10 min, filtrated, neutralized with diluted sulfuric acid, and concentrated under reduced pressure. The residue was acidified to pH 2 and extracted with ethyl acetate. The organic phase was dried ($MgSO_4$) and evaporated to give a yellow oil (4.60 g), which was purified by preparative HPLC (nucleosil N, 5 M, hexane/2-propanol, 98/2, flow 40 mL/min, 40 bar) to give **17b** (2.50 g, 50%) and **19** (1.25 g, 25%) as viscous colorless oils. **17b**: $[\alpha]^{20}_D$ +6.8° (c 1). IR (film): 3500, 3100, 3060, 3030, 2950, 1730, 1590, 1490, 1450, 1260, 1060, 950, 700, 630 cm^{-1}: ^1H NMR: δ 1.04 (d, J = 7.0 Hz, 6 H, 4- and 6-CH_3), 1.32 (s 3 H, 2-CH_3), 2.08 (m, 1 H, H-6), 2.19 (m, 1 H, H-4), 2.82 (d, J = 7.0 Hz, 1 H, 3-OH), 3.13 (d, J = 6.0 Hz, 2 H, H-7), 3.54 (s, 1 H, 2-OH), 3.66 (dd, J = 6.0 Hz, J = 4.5 Hz, 1 H, H-5), 3.74 (s, 3 H, OCH_3), 3.92 (d, J = 7.5 Hz, 1 H, H-3); AB system (δ_A 4.38, δ_B 4.43, J_{AB} = 10.0 Hz, 2 H, -OCH_2 = Ph), 7.19 (m, 15 H, phenyl-H), 7.45 (m, 5 H, phenyl-H). ^{13}C NMR: δ 8.37 and 12.12 (4-CH_3 and 6-CH_3), 21.97 (2-CH_3), 35.72 and 36.34 (C-4 and C-6), 52.61 (1-OCH_3), 66.25 (C-7), 73.95 and 75.81 (C-5 and 5-OCH_2-), 77.39 (C-2), 83.80 (C-5), 86.21 (C-5), 126.61, 127.12, 127.30, 127.42, 127.91, 128.39, 138.05 and 143.88 (20 phenyl-C), 176.58 (C-1). Anal. Calcd for $C_{37}H_{42}O_6$: C, 76.26; H, 7.26. Found: C, 76.77; H, 7.39.

19: $[\alpha]^{20}_D$ −15.6° (c 5). ^1H NMR: δ 0.95 (d, J = 7.2 Hz, 3 H, CH_3), 1.01 (d, J = 7.2 Hz, 3 H, CH_3), 1.20 (s, 3 H, CH_3, 1.95 (m, 1 H, H-6), 2.08 (m, 1 H, H-4); AB part of ABX system (δ_A 2.96, δ_B 3.05, J_{AB} = 9.5 Hz, J_{AX} = J_{BX} = 5.7 Hz, 2 H, H-7), 3.40 (s, 1 H, 2-OH), 3.64 (s, 3 H, OCH_3), 3.68 (dd, J = 2.8 Hz, J = 6.8 Hz, 1 H, H-5), 3.97 (d, J = 7.5 Hz, 1 H, 3-OH), 4.23 (dd, J = 5.0 Hz, J = 2.3 Hz, 1 H, H-3); AB system (δ_A 4.34, δ_B 4.44, J_{AB} = 11.5 Hz, 2 H, -OCH_2Ph), 7.13 (m, 15 H, phenyl-H), 7.36 (m, 5 H, phenyl-H). ^{13}C NMR: δ 13.42 and 13.98 (4- and 6-CH_3), 21.86 (2-CH_3), 35.58 and 37.12 (C-4 and C-6), 52.78 (OCH_3), 66.87, 72.38, 79.35, and 81.13 (C-7, C-3, C-2, and -OC_2Ph), 86.53 (C-5), 126.87, 127.31, 127.42, 127.66, 128.29, 128.70, 138.29, and 144.09 20 Ar C), 176.85 (C-1).

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Regioselectivity of Addition of Thiols and Amines to Conjugated Allenic Ketones and Esters

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Regioselectivity of nucleophilic addition to conjugated allenic ketones depends strongly on the nucleophile: anionic nucleophiles, e.g., triethylamine salts of benzenethiols, gave the β-substituted β,γ-unsaturated ketones with high selectivity. In contrast, neutral nucleophile molecules, e.g., benzenethiols or aniline, afforded the β-substituted α,β-unsaturated ketones. The reactions to allenecarboxylic esters indicated the same regiochemical tendency, but lower selectivities were observed in the reactions with benzenethiol.

Nucleophilic addition reactions to conjugated allenic carbonyl compounds have become of interest in relation to the mode of reaction of "suicide enzyme inhibitors".[1] It is well-known that the allenic groups conjugated to an electron-withdrawing substituent readily undergo nucleophilic addition reactions. However, there have been conflicting reports on the regiochemical selectivity of the reaction.[2] Allenic ketones and esters were shown to yield β-alkoxy- and β-amino α,β-unsaturated adducts by their

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