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# Chemo-enzymatic synthesis of (−)-epipentenomycin I

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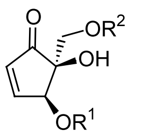
**Abstract**—A chemo-enzymatic synthesis of (−)-epipentenomycin I is reported using a lipase-catalysed kinetic resolution of the racemic pentacyclic alcohol **8**. Flash vacuum pyroloysis of (−)-**8** so obtained gave (−)-(4*R*)-4-hydroxy-5-methylene-2-cyclopentenone. Epoxidation of this compound with dimethyldioxirane followed by hydrolytic ring-opening of the resulting epoxide gave (−)-epipentenomycin I.

## 1. Introduction

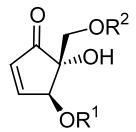
The pentenomycin group of natural products **1**–**4** have antibacterial activities against both Gram-positive and Gram-negative bacteria. Pentenomycins I **1** and II **2** were first isolated from *Streptomyces eurythermus* in 1973[1] while pentenomycin III **3** was isolated 3 years later from *Streptoverticillium eurocidicum*.[2] Epipentenomycin I **4**, however, was isolated in 1989[3a] from carpophores of *Perziza sp*., much later than its first synthesis in racemic form in 1980.[4,5] This compound was shown to have the (4*S*,5*R*) absolute configuration by X-ray crystallographic analysis of its 2-bromo-*O*-triacetate derivative,[3b] thus establishing that pentenomycin I **1** and epipentenomycin I **4** are epimeric at C-5. Their biological activities and their highly oxygenated structures have attracted several synthetic studies on their total synthesis,[6] the synthesis of their racemates[4,5,7] and their analogues,[8] e.g. epipentenomycin II **5** and III **6**. We recently reported a diastereoselective synthesis of (±)-epipentenomycin I **4** and III **6** from the diastereoselective epoxidation of 4-hydroxy- and 4-acetoxy-5-methylene-2-cyclopentenone, respectively, with dimethyldioxirane followed by hydrolytic ring-opening of the resulting epoxide.[7c] We now report a chemo-enzymatic synthesis of (−)-(4*R*,5*S*)-epipentenomycin I via (−)-(4*R*)-4-hydroxy-5-methylene-2-cyclopentenone.

## 2. Results and discussion

The known racemic epoxide, *rac*-**7**[9] (a 1.6:1 mixture of diastereomers), was converted to a mixture the known racemic alcohols *rac*-**8** and *rac*-**10** (Scheme 1).[9] These isomers could be obtained pure after separated by column chromatography and recrystallization. The relative stereochemistry of these compounds was determined by NOESY experiments and single crystal X-ray analysis on their corresponding acetates *rac*-**9** and *rac*-**11**, respectively.[10] NOESY studies on *rac*-**9** showed cross-peaks between the allylic proton Ha and the benzylic methine Hb, while in *rac*-**11**, cross-peaks were observed between the allylic proton Hb and one methylene proton Ha (Scheme 1). Kinetic resolution of *rac*-**8** was achieved using PS-D 'Amano' I lipase on Celite and vinyl acetate (6 equiv.) in acetonitile at 40°C. After



**1**; pentenomycin I ($R^1 = R^2 = H$)
**2**; pentenomycin II ($R^1 = Ac$, $R^2 = H$)
**3**; pentenomycin III ($R^1 = H$, $R^2 = Ac$)



**4**; epipentenomycin I ($R^1 = R^2 = H$)
**5**; epipentenomycin II ($R^1 = Ac$, $R^2 = H$)
**6**; epipentenomycin III ($R^1 = H$, $R^2 = Ac$)

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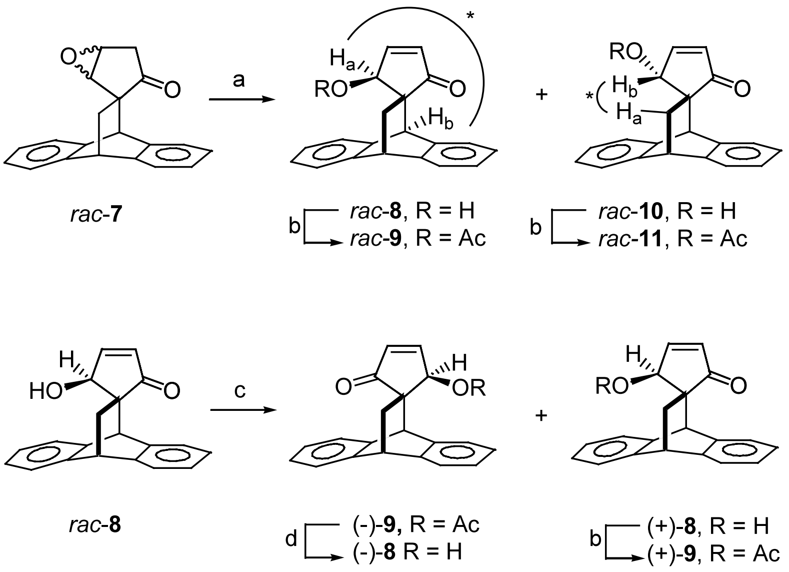


**Scheme 1.** * indicates NOESY cross peaks. *Reagents and conditions*: (a) $Et_3N$, $CH_2Cl_2$, 0°C to rt, 16 h; (b) $Ac_2O$, pyridine; (c) PS-D 'Amano' I lipase on Celite, vinyl acetate, MeCN, 40°C, 101 h; (d) TFA, MeCN, $H_2O$, 60°C 16 h.

101 h the reaction was terminated at 41% conversion.[11] The reaction mixture was separated by column chromatography to provide acetate (−)-**9** {$[\alpha]_D^{24}=-189$ (*c* 2.03, $CHCl_3$)}, in 37% yield and in greater than 98% enantiomeric excess, and the alcohol (+)-**8** in 53% yield and 68% enantiomeric purity, as determined on its acetate (+)-**9**. The enantiomeric excesses of (−)-**9** and that of (+)-**9** were determined by $^1H$ NMR using the chiral shift reagent, europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate] ($Eu(hfc)_3$, see Section 3 (general remarks) for specific details).

While base catalysed hydrolysis ($K_2CO_3$, MeOH) of acetate (−)-**9** resulted in Michael addition of methanol to the enone of (−)-**8**, acid catalysed hydrolysis using aqueous trifluoroacetic acid in acetonitile smoothly gave the desired alcohol (−)-**8** {$[\alpha]_D^{24}=-120$ (*c* 1.28, $CHCl_3$)} in excellent yield (96%) (Scheme 1).

Flash vacuum pyrolysis of (−)-**8** at 450°C and <0.1 mmHg gave (−)-(4*R*)-4-hydroxy-5-methylene-2-cyclopentenone, (−)-**12**, in 76% yield. Treatment of this compound with freshly distilled dimethyldioxirane (DMDO) in acetone[12] initially at −78°C and then at rt for 16 h produced an 83:17 mixture of the *anti*- and *syn*-epoxy-alcohols, respectively. The crude mixture was separated by flash chromatography to give about a 90:10 mixture of these isomers. Recrystallization of this mixture gave pure (−)-(3*S*,7*R*)-**13** in 39% yield (mp 94–95°C) from which single crystals were obtained. X-Ray crystallographic analysis (Fig. 1) confirmed our earlier NOESY NMR experiments that the major diastereomer resulted from epoxidation of (−)-**12**, *anti* to the allylic hydroxy group.[7c,10]

Heating a solution of (−)-**13** in water[7c,13] in a sealed tube at 80°C, with monitoring by $^1H$ NMR spectroscopy, cleanly led to ring-opening of the epoxide group. After freeze-drying (−)-epipentenomycin I, (−)-**4** was obtained in 86% yield (Scheme 2). This sample had identical spectral

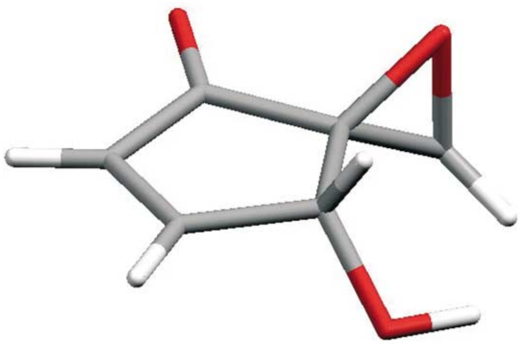
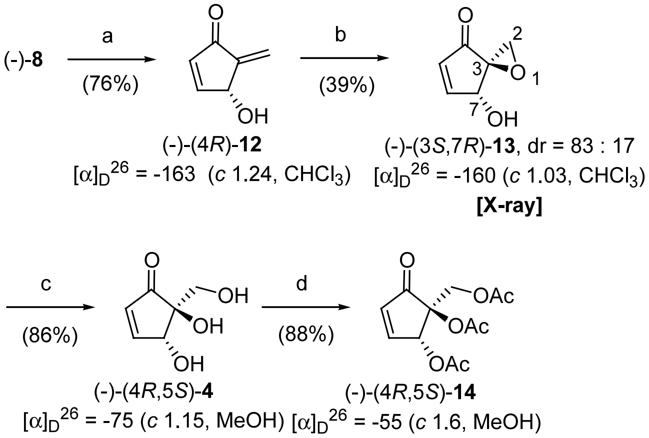


**Figure 1.** Single-crystal X-ray crystallographic structure of (−)-**13**.[10]



**Scheme 2.** *Reagents and conditions*: (a) FVP (450°C, <0.1 mmHg); (b) dimethyldioxirane, acetone, −78°C to rt, 16 h; (c) $H_2O$, 80°C, 16 h; (d) $Ac_2O$, pyridine, rt, 16 h.

characteristics to those reported in the literature for (+)-**4**,[3b,7a] however its specific rotation was opposite in sign {$[\alpha]_D^{26} = -75$ (*c* 1.15, MeOH), lit.[3b] ($[\alpha]_D^{23} = +35.3$ (*c* 2.6, MeOH)} and larger in magnitude than the literature value. This discrepancy in the magnitude of the specific rotations may be due to the hydroscopic nature of these compounds and therefore (−)-**4** was converted to the known and less hydroscopic triacetate (−)-**14** (Scheme 2). This sample had identical spectral characteristics to those reported in the literature for (+)-**14**,[3b,7a] and the magnitude of its specific rotation was similar to the literature value {$[\alpha]_D^{26} = -55$ (*c* 1.16, MeOH), lit.[3b] ($[\alpha]_D^{23} = +47$ (*c* 0.21, MeOH)}.

In conclusion we have developed an efficient chemoenzymatic synthesis of (−)-epipentenomycin I using a lipase catalysed kinetic resolution of the racemic pentacyclic alcohol *rac*-**8**. The chiral chemical intermediates described here should be valuable for the synthesis of other bioactive molecules and we are currently investigating their chemistry.

## 3. Experimental

### 3.1. General remarks

All NMR spectra were determined in solutions of $CDCl_3$ at 300 MHz ($^1H$ NMR) or 75 MHz ($^{13}C$ NMR) unless otherwise stated. NMR assignments are based upon 2D NMR spectral analysis (COSY and DEPT). Lipase used in this experiment was PS-D Amano I (immobilized PS-D 'Amano' I lipase on Celite) from Amano Enzyme Inc., Japan. To determine the enantiomeric excess of the enzymatically resolved alcohols, they were converted in to their acetates **9** with acetic anhydride/pyridine. The enantiomeric excess was determined by $^1H$ NMR using the chiral shift reagent, europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate]. The acetate **9** (5.0 mg) was dissolved in 0.7 mL of a solution of Eu(hfc$_3$) (14.8 mg) in $CDCl_3$ (5.0 mL). The acetate signals of (+)-**9** and (−)-**9** were at $\delta$ 1.872 and 1.877, respectively.

### 3.2. 9′,10′-Dihydro-5-hydroxy-spiro[3-cyclopenten-1,11′-(9,10)ethanoanthracene]-2-one *rac*-8 and *rac*-10

To a solution of the crude epoxide *rac*-**7**[9] (dr = 1.6:1 was indicated by $^1H$ NMR) (1.50 g, 5.21 mmol) in dry $CH_2Cl_2$ (20 mL) at 0°C was added triethylamine (1.5 mL, 10.42 mmol) and the resulting mixture was stirred at rt overnight. Solvents were evaporated to dryness and the diastereomeric alcohols were separated by column chromatography on silica gel ($CH_2Cl_2$: petroleum spirit; 9:1 as the eluent). Recrystallization from $CH_2Cl_2$ and petroleum spirit gave *rac*-**8** (0.843 g, 2.927 mmol) and *rac*-**10** (0.552 g, 1.9167 mmol). ***rac*-8**: White crystals, mp 162–163°C (from $CH_2Cl_2$/petroleum spirit) (lit.[14] 163–165°C, from $CH_2Cl_2$/hexane). IR ($CHCl_3$), $\nu_{max}$, 3415, 3025, 2933, 1709, 1460, 1170, 763 cm$^{-1}$. $^1H$ NMR $\delta$ 0.86 (br d, OH, 1H), 1.78, 2.30, 4.40 (ABX system, $J_{AB} = 12.7$Hz, $J_{AX} = J_{BX} = 2.5$ Hz, 3H), 3.99 (s, 1H), 4.57–4.60 (m, 1H), 6.19 (dd, $J = 7.5$, 1.5 Hz, 1H), 7.05–7.50 (m, 9H). $^{13}C$ NMR $\delta$ 34.3, 44.5, 52.1, 56.7, 78.2, 123.0, 124.2, 124.7, 125.9, 126.0, 126.3, 126.5, 126.8, 134.2, 139.8, 141.6, 144.5, 144.6, 160.0, 208.3. LRMS (CI +ve) (isobutane): 288 $[M]^+$ (2%), 178 $[C_{14}H_{10}]^+$ (100%). HRMS (CI +ve) calcd for $C_{20}H_{16}O_2$ $[M]^+$ 288.115082. Found: 288.115030. ***rac*-10**: White crystals, mp 159–160°C (from $CH_2Cl_2$/hexane) (lit.[14] 159–160°C from $CH_2Cl_2$/hexane). IR ($CHCl_3$), $\nu_{max}$, 3450, 3030, 2933, 1710, 1680, 1440, 1325, 765 cm$^{-1}$. $^1H$ NMR $\delta$ 2.09 (br d, OH, 1H), 1.73, 2.04, 4.38 (ABX system, $J_{AB} = 12.3$ Hz, $J_{AX} = J_{BX} = 2.7$ Hz, 3H), 4.23–4.25 (m, 1H), 4.35–4.37 (m, 1H), 6.19 (dd, $J = 6$, 0.9 Hz, 1H), 7.06–7.43 (m, 9H). $^{13}C$ NMR $\delta$ 41.0, 44.4, 47.7, 56.3, 81.0, 122.9, 123.8, 125.2, 125.5, 125.7, 125.8, 126.0, 126.2, 134.7, 140.3, 141.7, 143.9, 145.0, 159.0, 207.3.

### 3.3. Kinetic resolution of 9′,10′-dihydro-5-hydroxy-spiro[3-cyclopenten-1,11′-(9,10)ethanoanthracene]-2-one *rac*-8

To a solution of *rac*-**8** (1.000 g, 3.47 mmol) and vinyl acetate (1.9 mL, 20.82 mmol) in acetonitrile (35 mL) was added immobilized PS-D 'Amano' I Lipase on Celite (2.000 g). After 101 h at 40°C, with stirring at 400 rpm, 41% conversion was calculated from the enantiomeric excess of the starting alcohol **8** and the acetate **9** according to % conv. = 68/(68+98) = 41.[11] The reaction mixture was diluted in $CH_2Cl_2$, filtered through a plug of Celite and evaporated to dryness. The crude mixture was purified by column chromatography on silica gel. Elution with 30% petroleum spirit in $CH_2Cl_2$ gave the acetate (−)-**9** (0.42 g, 37%, ee >98%). The column was then stripped with 20% EtOAc in $CH_2Cl_2$ to obtain the alcohol (+)-**8** (0.53 g, 53%, ee = 68%). The alcohol (+)-**8** (0.53 g) was recrystallized from $CH_2Cl_2$/petroleum spirit to obtain (+)-**8** (0.33 g, 33%, ee >98%). (+)-**8**: White crystals, mp 166–167°C (from $CH_2Cl_2$/petroleum spirit). $[\alpha]_D^{24} = +119.7$ (*c* 1.98; $CHCl_3$), ee >98%. Spectral data were identical to *rac*-**8**. (−)-**9**: White crystals; mp 210–211°C (from $CH_2Cl_2$/petroleum spirit), $[\alpha]_D^{24} = -189.2$ (*c* 2.03, $CHCl_3$), ee >98%. $^1H$ NMR: $\delta$ 1.74 (s, 3H), 1.89, 2.11, 4.38 (ABX system, $J_{AB} = 12.7$ Hz, $J_{AX} = J_{BX} = 2.4$ Hz, 3H), 3.99 (s, 1H), 5.49 (dd, $J = 2.7$, 1.2 Hz, 1H), 6.30 (dd, $J = 6.0$, 0.6 Hz, 1H), 7.11–7.33 (m, 8H), 7.45 (dd, $J = 6.0$, 2.7 Hz, 1H). $^{13}C$ NMR $\delta$ 20.6, 34.5, 44.5, 52.4, 55.3, 78.8, 123.1, 123.8, 125.2, 125.9, 126.3, 126.7, 126.8, 135.6, 139.6, 140.9, 144.3, 144.6, 156.6, 169.8, 207. LRMS (CI +ve) (isobutane): 331 $[M+H]^+$ (7%), 271 (65%), 179 $[C_{14}H_{10}+H]^+$ (100%). HRMS (CI +ve) calcd for $C_{22}H_{18}O_3$ $(M)^+$ 330.124909. Found: 330.125595.

### 3.4. (−)-9′,10′-Dihydro-5-hydroxy-spiro[3-cyclopenten-1,11′-(9,10)ethanoanthracene]-2-one (−)-8

To a solution of (−)-**9** (372 mg, 1.125 mmol) in $CH_3CN/H_2O$ (3:1, 16 mL) was added TFA (2.9 mL, 3.94 mmol). The reaction mixture was then heated overnight at 60°C. The aqueous layer was extracted with $CH_2Cl_2$ (3×15 mL) and the organic layers were washed with water, brine and dried ($MgSO_4$). The solvent was evaporated to dryness and the residue was purified by flash column chromatography on silica gel using 20% EtOAc in $CH_2Cl_2$ as the eluent to give the alcohol (−)-**8** (311 mg, 96%). (−)-**8**: white crystals; mp 162–163°C ($CH_2Cl_2$/pretoleum spirit), $[\alpha]_D^{27} = -120$ (*c* 1.28; $CHCl_3$). Spectral data were identical to *rac*-**8**.

### 3.5. (−)-(4*R*)-4-Hydroxy-5-methylene-2-cyclopentenone (−)-12

Compound (−)-**8** (390 mg, 1.354 mmol; 30 mg was used each time) was placed in 10 mL round-bottom flask connected to a gas phase pyrolysis apparatus and the system was subjected to high vacuum (<0.1 mmHg). The sample was carefully pyrolysed with heat gun and the vapour passed through the heating column at 450°C. The crude product was purified by flash column chromatography on silica gel, elution with petroleum spirit gave (−)-**12** (113.9 mg, 76%) that was homogeneous from TLC and NMR analysis. This compound was used immediately in the next step or could be stored for a few days in the freezer without noticeable polymerization. (−)-**12**: viscous liquid, $[\alpha]_D^{26} = -163.3$ (*c* 1.24, $CHCl_3$), IR (neat) $\nu_{max}$ 3403, 2876, 1705, 1579, 1400, 895 $cm^{-1}$. $^1H$ NMR $\delta$ 2.42–2.56 (br, OH, 1H), 5.22 (s, 1H, H-4), 5.76 (s, 1H, $=C\underline{H}H$), 6.20 (s, 1H, $=C\underline{H}H$), 6.45 (dd, $J = 6.5$, 0.9 Hz, 1H, H-2), 7.54 (ddd, $J = 6.0$, 2.4, 0.9 Hz, 1H, H-3). $^{13}C$ NMR $\delta$ 70.7 (C-4), 119.0 (C-6), 136.2 (C-2), 145.1 (C-5), 159.6 (C-3), 194.8 (C-1). CIMS (isobutane): 111 $[M+H]^+$ (100%).

### 3.6. (−)-(3*S*,7*R*)-7-Hydroxy-1-oxaspiro[2.4]hept-5-en-4-one (−)-13

To a solution of (−)-**12** (62.1 mg, 0.565 mmol) in acetone (5 mL) was added a solution of freshly distilled dimethyldioxirane (21 mL, 1.491 mmol) in acetone at −78°C and the reaction was left to stir overnight at room temperature. The solvent was then evaporated to dryness. The crude product (dr = 83:17 from $^1H$ NMR analysis) was purified by flash column chromatography on silica gel using 10% EtOAc in petroleum spirit as the initial eluent followed by 20% EtOAc in petroleum spirit. Recrystallization from $CH_2Cl_2$ in the freezer (−20°C) gave pure (−)-**13** (28 mg, 39%). (−)-**13**: white crystals; mp 94–95°C (from $CH_2Cl_2$), $[\alpha]_D^{26} = -159.6$ (*c* 1.03; $CHCl_3$), $^1H$ NMR $\delta$ 2.51 (br d, $J = 7.5$ Hz, OH, 1H), 3.14 (d, $J = 6.6$ Hz, 1H, $C\underline{H}HO$), 3.29 (d, $J = 6.9$ Hz, 1H, $C\underline{H}HO$), 4.95 (br s, 1H, H-7), 6.52 (dd, $J = 6.3$, 1.5 Hz, 1H, H-5), 7.70 (dd, $J = 6.3$, 2.4 Hz, 1H, H-6). $^{13}C$ NMR $\delta$ 51.1 (C-2), 64.2 (C-3), 71.0 (C-7), 135.9 (C-5), 161.8 (C-6), 199.8 (C-4). LRMS (CI +ve) (isobutane): 127 $[M+H]^+$ (100%), 109 $[M-H_2O]^+$ (37%), 81 (15%). HRMS (CI +ve) calcd for $C_6H_7O_3$ $(M+H)^+$ 127.040235. Found: 127.039519.

### 3.7. (−)-(4*R*,5*S*)-Epipentenomycin I (−)-4

A solution of (−)-**13** (14.5 mg, 0.115 mmol) in $H_2O$ (0.5 mL) was heated overnight at 80°C. The water was then evaporated under vacuo to obtain (−)-**4** (14.3 mg, 86%) that was pure by TLC and NMR analysis. (−)-**4**: viscous liquid $[\alpha]_D^{26} = -75.3$ (*c* 1.15; MeOH), IR (neat) $\nu_{max}$, 3381, 2928, 2532, 1711, 1657, 1253, 1058, 840 $cm^{-1}$. The $^1H$ and $^{13}C$ NMR of this compound was identical to that reported in the literature.[3] $^1H$ NMR ($D_2O$): $\delta$ 3.71 (d, $J = 12$ Hz, 1H, $C\underline{H}HOH$), 3.82 (d, $J = 12$ Hz, 1H, $C\underline{H}HOH$), 4.86 (m, 1H, H-4), 6.41 (dd, $J = 6.3$, 1.5 Hz, H-2), 7.73 (dd, $J = 6.3$, 2.1 Hz, H-3). $^{13}C$ NMR ($D_2O$+ MeCN as internal standard): $\delta$ 63.6 (C-6), 77.5 (C-4), 82.4 (C-5), 132.5 (C-2), 163.8 (C-3), 208.5 (C-1). LRMS (CI +ve): 145 $[M+H]^+$ (100%), 127 $[M-H_2O]^+$ (26%). HRMS (CI +ve) calcd for $C_6H_9O_4$ $(M+H)^+$ 145.050356. Found: 145.050084.

### 3.8. (−)-(4*R*,5*S*)-Epipentenomycin I triacetate (−)-14

A solution (−)-**4** (11.3 mg, 0.079 mmol) in pyridine (2 mL) was added excess acetic anhydride at room temperature and the reaction mixture was left to stir overnight. The solvents were then evaporated to dryness. The crude product was purified by flash column chromatography on silica gel using 30% EtOAc in petroleum sprit as the eluent to obtain (−)-**14** (18.7 mg, 88%). (−)-**14**: viscous liquid, $[\alpha]_D^{26} = -55.1$ (*c* 1.16; MeOH) lit.[3] $[\alpha]_D^{23} = +47.5$ (*c* 0.64; MeOH). IR (neat) $\nu_{max}$ 2923, 2360, 1735, 1374, 1214, 1054 $cm^{-1}$. The $^1H$ and $^{13}C$ NMR of this compound was identical to that reported in the literature.[3] $^1H$ NMR $\delta$ 2.14, 2.13 and 2.04 (s, 3×3H, OAc), 4.07 (d, $J = 12$ Hz, 1H, $C\underline{H}HOAc$), 4.52 (d, $J = 12$ Hz, 1H, $C\underline{H}HOAc$), 6.26 (m, 1H, H-4), 6.49 (dd, $J = 6.3$, 1.8 Hz, 1H, H-2), 7.38 (dd, $J = 6.3$, 2.4 Hz, 1H, H-3). $^{13}C$ NMR $\delta$ 197.3 (C-1), 170.2, 170.1 and 170.0 (CO-acetyls), 155.0 (C-3), 134.9 (C-2), 82.8 (C-5), 77.2 (C-4), 62.5 (C-6), 20.8 (Me-acetyls). LRMS (CI +ve): 271 $[M+H]^+$ (100%). HRMS (CI +ve) calcd for $C_{12}H_{15}O_7$ $(M+H)^+$ 271.082469. Found: 271.081778.

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10. *rac*-**9** and *rac*-**11** correspond to structures **12a** (CCDC# 184071) and **12b** (CCDC# 184072) of Ref. 7c (crystal/refinement details not given in Ref. 7c). For these two isomers of $C_{22}H_{18}O_3$, $M_r = 330.4$ at ca.0 153 K. *rac*-**9**: Monoclinic, space group $P2_1$ (note that although this space group is chiral, the bulk sample is racemic), $a = 8.132(1)$, $b = 9.697(1)$, $c = 10.898(2)$ Å, $\beta = 103.344(4)°$, $V = 836$ Å$^3$, $Z = 2$. $R = 0.050$, $R_w = 0.051$, for $N_o = 1671$ CCD reflections ($F > 4\sigma(F)$), Mo Kα radiation) (chirality indeterminate) (CCDC# 184071). *rac*-**11**: Monoclinic, $P2_1/c$ (i.e. racemic specimen), $a = 9.592(2)$, $b = 17.638(4)$, $c = 10.078(2)$ Å, $\beta = 103.265(4)°$, $V = 1160$ Å$^3$, $Z = 4$. $R = 0.049$, $R_w = 0.056$, for $N_o = 1981$ (CCDC# 184072)). (−)-**13** is monoclinic, $P2_1$, $a = 6.906(3)$, $b = 10.971(4)$, $c = 7.212(3)$ Å, $\beta = 95.157(6)°$, $V = 544$ Å$^3$, $Z = 4$. $R = 0.086$, $R_w = 0.010$, for $N_o = 1176$ (CCDC# 212132). The chirality adopted is assigned from chemistry. The material was 'difficult', presumably in consequence of the packing of the molecules in strings, each made up of symmetry-related sequences of the independent components molecule 1 *or* molecule 2 of the asymmetric unit, linked by hydrogen-bonds between the hydroxyl hydrogen of one molecule and the ketonic oxygen of the next.
11. The percentage conversion was calculated from the enantiomeric excess of the starting alcohol **8** and acetate **9** according to % conv. = 68/(68+98) = 41. See: Chen, C.-S.; Fujimoto, Y.; Girdaukas, G.; Sih, C. J. *J. Am. Chem. Soc.* **1982**, *104*, 7294.
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