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A New Approach to the Synthesis of Chiral Vinyl Carbinols from 2,3-Epoxy Alcohols

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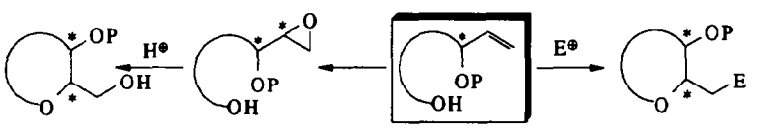
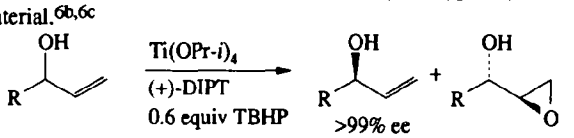
Abstract: The regioselective opening with benzoic acid of 2,3-epoxy alcohols obtained from the asymmetric epoxidation of 2,3-allylic alcohols, and deoxygenation of the resulting diol benzoates provides an effective, general and simple method to convert chiral 2,3-epoxy alcohols, into vinyl carbinols without the loss of any optical purity.

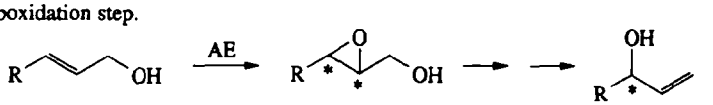
In the course of our synthetic studies directed to the enantiomeric synthesis of bioactive natural compounds, we have focussed our interest on a wide range of substances containing polyfunctionalized cyclic ethers.[1] This structural feature may be the cause of the strong bioactivity of substances such as polyether marine toxins,[2] ionophore antibiotics[3] and other naturally occurring compounds.[4] We have considered that a useful way to obtain such cyclic units in a stereochemically controlled manner would be the electrophilic cyclization of the suitable hydroxy vinyl alcohols,[5] or the intramolecular opening of epoxy alcohols.[5a]



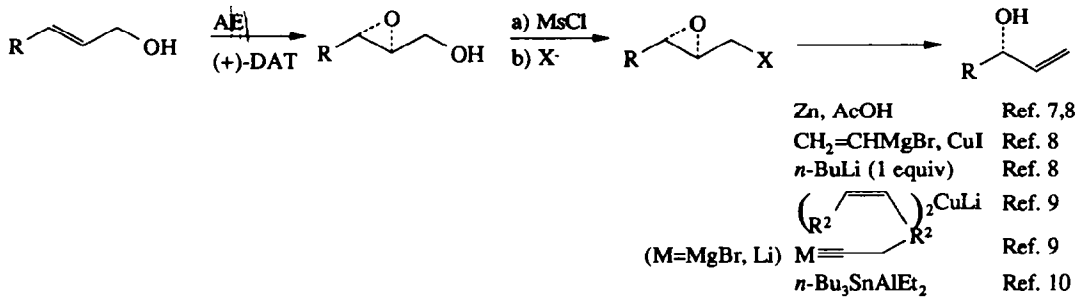
Chiral vinyl carbinols of extremely high enantiomeric purity are typically obtained by the kinetic resolution of the racemic material.[6b,6c]



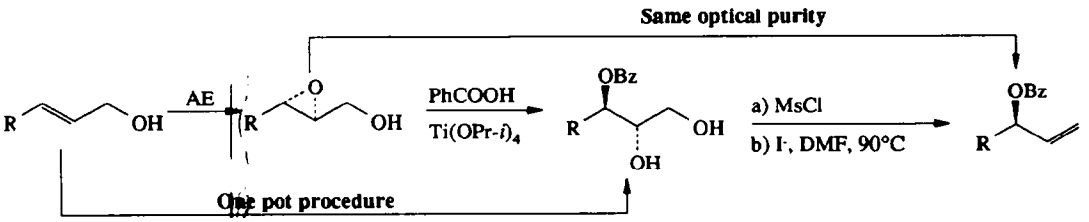
Since the maximum theoretical yield in a resolution procedure is 50%, efforts have been made in order to obtain the vinyl carbinol unit by adequate transformations of the 2,3-epoxy alcohols obtained by the Sharpless asymmetric epoxidation of a very wide range of 2,3-allylic alcohols,[6] retaining the optical purity reached in the epoxidation step.



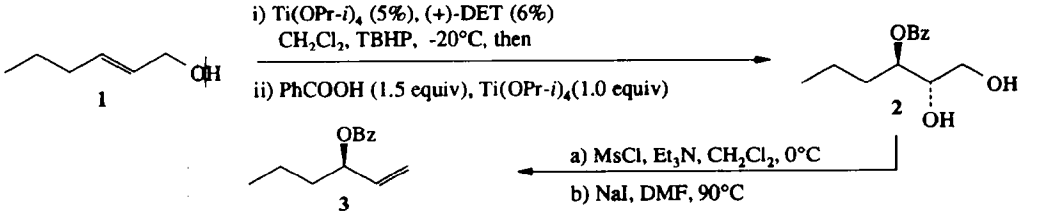
Such conversions have been successfully accomplished via the corresponding epoxy halides by acidic[7,8,10] or basic[8,9] eliminations.



In this paper we present an alternative approach to the above described conversion which makes use of a regioselective opening with benzoic acid in the C-3 position and further elimination of the resulting diol benzoate. 2,3-Epoxy alcohols can be regioselectively opened with carboxylic acid using titanium tetraisopropoxide as a stoichiometric catalyst.[1c,11,12] The combination of such an opening procedure with a suitable deoxygenating method of the diol obtained[13] provides a way to achieve the desired conversion.

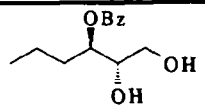
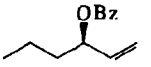
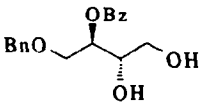
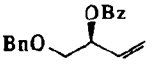
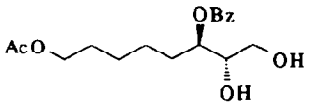
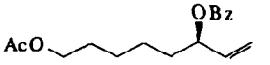
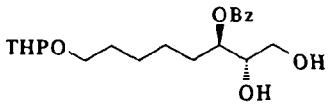
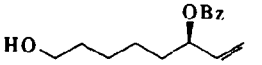
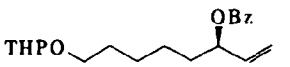
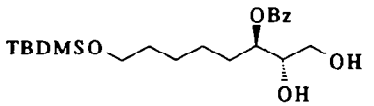
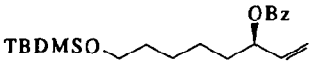
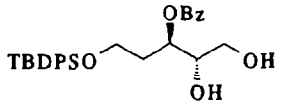
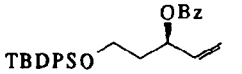
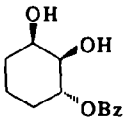
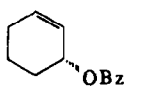


To achieve the highest conversion and yield we have performed the asymmetric epoxidation in the catalytic manner[6c] in order to perform the opening of the formed 2,3-epoxy alcohol without any isolation step. This methodology takes full advantage of the main feature of the catalytic asymmetric epoxidation, the "in situ" derivatization.[6c] From the existing methods found in the literature[13] we considered that the elimination of vicinal disulfonyloxy groups by treatment with sodium iodide was the most convenient for our purposes. Thus, after the asymmetric epoxidation step was completed a full equivalent amount of Ti(OPr-*i*)$_4$ and benzoic acid were added to the reaction mixture yielding a crude diol benzoate which without any purification was sequentially mesylated and treated with a NaI solution in DMF, until complete deoxygenation was observed. The complete sequence led to the vinyl benzoate with yields ranging from 60 to 75%.



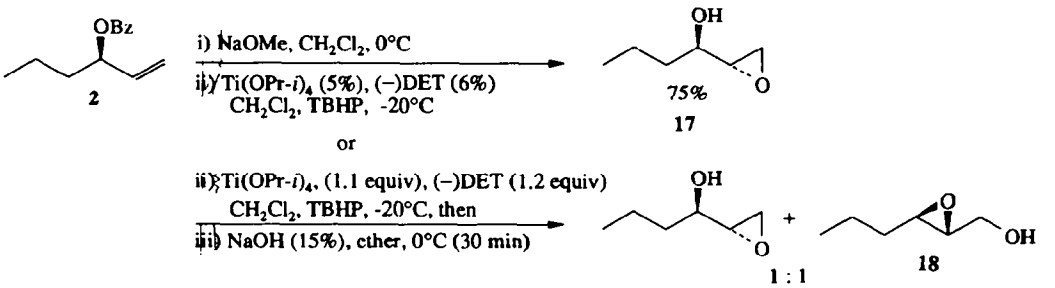
When the sequence was applied to systems containing hydroxyl protecting groups such as tetrahydropyranyl, *tert*-butyldimethylsilyl or *tert*-butyldiphenyl silyl ethers we found that the removal of these groups was produced jointly with the elimination procedure. Although this removal is very useful for our purposes we have also investigated the possibility of avoiding an associated reaction of this type. In order to avoid a reaction of this nature the deoxygenation steps were performed by preparing the trifluoromethanesulphonate esters which without isolation were treated with a solution of NaI in DMF. The results obtained for a few examples using both methods over the pure diol benzoates are summarized in **Table I.**

Table I. Elimination of chiral 1,2-diol-3-benzoates to vinyl carbinol benzoates

Entry	Compound[a)]	Method[b)]	Product	Yield
1.	 **2**	A	 **3**	85
		B		60
2.	 **4**	A	 **5**	90
		B		60
3.	 **6**	A	 **7**	82
		B		61
4.	 **8**	A	 **9**	80
		B	 **10**	53
5.	 **11**	B	 **12**	66
6.	 **13**	A	 **14**	22
		B		60
7.	 **15**	B	 **16**	60

a) All materials were used in optically active form (≥93% ee)[14], except entry 7 (racemic).
b) See the Experimental Section.

In order to attain a more complete application of the above described sequence we decided to obtain the terminal epoxy alcohols in a stereoselective manner from the vinyl carbinol benzoate. The removal of the benzoate group under standard conditions (NaOMe, CH_2Cl_2) led quantitatively to the allylic alcohol which under catalytic asymmetric epoxidation afforded the expected diastereoisomer *erythro*-1,2-epoxy alcohol **17** $[\alpha]_D^{25}$ −24.4 (c 1.03, $CHCl_3$) as the only detectable product. However, when the asymmetric epoxidation was executed in a stoichiometric manner over the free alcohol a substantial amount of the 2,3-epoxy alcohol **18** $[\alpha]_D^{25}$ +39.5 (c 1.3, $CHCl_3$) [Lit.[15] $[\alpha]_D^{25}$ +40.8 (c 1.3, $CHCl_3$)] was produced, after the alkaline treatment was performed to remove the tartrate esters.[16]



Considering the possibility of the isomerization of such *erythro*-epoxy alcohols to the *threo*-isomer[17] a more complete control of the products obtained from the asymmetric epoxidation is achieved. On the other hand, with these methods we are now able to obtain precursors for use in the synthesis of functionalized cyclic ethers. Further applications of this method will be published elsewhere.

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Experimental Section

Materials and Methods:

^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AMX 400 spectrometer in $CDCl_3$ as solvent and chemical shifts are reported relative to Me_4Si. Low resolution mass spectra were obtained from a VG Micromass Zab-2F spectrometer. Optical rotations were determined for solutions in chloroform with a Perkin-Elmer Model 241 polarimeter. Infrared spectra were recorded on a Perkin-Elmer Model 1600FTIR spectrophotometer. Column chromatography was performed on silica gel, 0.063-0.2 mm, and T.L.C. was performed on silica gel, all Merck products. Visualization of spots was effected with U.V. light and/or phosphomolybdic acid in ethanol stain. All solvents were purified by standard techniques. Reactions requiring anhydrous conditions were performed under argon. Anhydrous magnesium sulphate was used for drying solutions.

General procedure to obtain enantiomerically enriched 1,2-diol benzoates from allylic alcohols. Synthesis of (2S, 3R)-3-benzoyloxy-1,2-hexanediol (2):

Crushed, activated 3Å molecular sieves (1.05g) were added to CH_2Cl_2 (250 mL), under argon atmosphere. The flask content was stirred and cooled to −20° C. Then $Ti(OPr\text{-}i)_4$ (0.9 mL, 859 mg, 3 mmol), (*E*)-2-hexen-1-ol (5 g, 50 mmol.) and L-(+)-DET (0.8 mL, 960 mg, 4.7 mmol) were added sequentially with stirring. The mixture was stirred for an additional 15 min., and TBHP (15.8 mL of a solution 5.7 M in isooctane) was added slowly. The cooled reaction mixture (20 °C) was stirred for 3 h until complete reaction (TLC). Then benzoic acid (3.3 g, 27 mmol) and $Ti(OPr\text{-}i)_4$ (14.88 mL, 14.2 g, 50 mmol) were added sequentially. The reaction was warmed to 0 °C and monitored by T.L.C. When completed, tartaric acid (150 mL of a 15% aqueous

solution) was added and the stirring was continued until clear phases were reached. The phases were separated, and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic phases were washed with saturated solution of $NaHCO_3$ and saturated brine, dried, concentrated and purified by column chromatography to yield **2** (9.53g, 40 mmol, 80% yield): $[\alpha]_D^{25}$ +24.1 (c 1.52, $CHCl_3$); ^1H NMR, δ: 0.94(t, J= 7.24 Hz, 3H) 1.46 (m, 2H), 1.62 (m, 2H), 3.65 (m, 3H), 5.13(m, 1H), 7.48 (m, 3H), 8.03 (m, 2H). ^{13}C NMR, δ: 13.63 (q), 16.60 (t), 32.74 (t), 62.61 (t), 73.13 (d), 74.73 (d), 128.42 (d), 129.69 (d), 133.28 (d), 167.12 (s); I.R. ($CHCl_3$) (cm^{-1}): 3469, 2962, 2875, 2357, 1700, 1451, 1280, 1115, 1070, 945, 842.; MS *m/z* (rel. int.): 204 [M^+], 106 (26), 83 [M^+-OBz], 77 (61).

General procedures for the elimination of the diol benzoates to vinyl carbinols. Synthesis of (3R)-benzoyloxy-1-hexene (3).

Method A: The diol benzoate **2** (3.67 g, 15.4 mmol) was dissolved in dry dichloromethane (100 mL) under argon atmosphere. The mixture was cooled to 0° C with an ice/ water bath. Once cooled, triethylamine (8.6 mL, 6.23 g, 4 equiv) and methylsulphonylchloride (3.33 mL, 4.9 g, 2.2 eq.) were added. The reaction was monitored by TLC until finished. Then the crude was poured over a beaker with a mixture of ice and 5% hydrochloric acid and subsequently extracted with ether. The organic phase was dried with anhydrous magnesium sulphate, filtered and concentrated. The obtained crude was dissolved in 90 mL of DMF and over this mixture was slowly added a solution of NaI (10 g, 62 mmol) in DMF (90 mL). The reaction mixture was warmed to 90° C for 1 h. The flask content was cooled to 0 °C and a saturated solution of sodium thiosulphate was added until the reaction mixture became colourless. Then the reaction mixture was extracted twice with ether and the combined organic phases were dried with anhydrous magnesic sulphate, filtered, concentrated and purified by column chromatography to yield **3** (2.67 g, 13.09 mmol, 85% yield): $[\alpha]_D^{25}$ −34.8 (c 5.1, $CHCl_3$); ^1H NMR, δ: 0.96 (t, J=7.24 Hz, 3H), 1.45 (m, 2H), 1.75 (m, 2H), 5.28 (m, 2H), 5.53 (m, 1H), 5.90 (m, 1H), 7.50 (m, 3H), 8.06 (m, 2H);^{13}C NMR, δ: 13.63 (q), 19.35 (t), 36.45 (t), 75.07 (d), 116.45 (t), 128.29 (d), 129.55 (d), 132.77 (d), 136.64 (d), 165.63 (s); I.R. ($CHCl_3$) (cm^{-1}): 2691, 2874, 2357, 1718, 1602, 1451, 1315, 1277, 1114, 902. MS *m/z* (rel. int.):204 [M^+], 106 (26), 83 [M^+-OBz], 77 (61).

Method B. Synthesis of (3R)-benzoyloxy-1-hexene (3) :

The diol benzoate **2** (890 mg, 3.7 mmol) was dissolved in dry CH_2CL_2 (30 mL) under argon atmosphere. The mixture was cooled to -30° C and pyridine (1.2 mL, 1.78 g) and trifluromethanesulfonylanhydride (1.6 mL, 2.28 g) were sequentially added. The reaction was monitored by TLC until completed. Then a solution of NaI (2.4 g, 16 mmol) in DMF (20 mL) was added. After 20 min, a saturated solution of sodium thiosulphate was added until the reaction mixture became colourless. Then the mixture was extracted twice with ether and the combined organic phases were dried, filtered, concentrated and purified by column chromatography to yield **3** (0.49 g, 2.22 mmol, 60% yield).

(2S, 3S)-1-Benzyloxy-2-benzoyloxy-3,4-butanediol (4) :

The general procedure to obtain 1,2-diol benzoates was used on (*E*)-1-benzyloxy-2-buten-4-ol (1.3 g, 7 mmol) yielding **4** (1.65 g, 5.25 mmol, 80%): $[\alpha]_D^{25}$ −47.3 (c 1.49, $CHCl_3$); ^1H NMR, δ: 3.77(m, 1H), 3.80 (m, 1H), 3.94 (m, 1H), 4.05 (m, 2H), 4.63 (m, 2H), 5.28 (m, 1H), 7.37(m, 5H), 7.52 (t, J=7.28 Hz, 2H), 7.63 (t, J=6.44 Hz, 1H), 8.09(d, J=7.24Hz, 2H). ^{13}C NMR, δ: 63.18 (t), 69.47 (t), 71.54 (d), 73.37 (d), 73.95 (t), 128.09 (d), 128.13 (d), 128.31 (d), 128.90 (d), 129.97 (d), 130.26 (d), 130.29 (d), 130.33 (d), 133.87 (d), 167.00 (s); IR ($CHCl_3$) (cm^{-1}): 3490, 3015, 2995, 1690, 1270, 1096; MS *m/z* (rel. int.): 317 [M^++1], 299 [M^+-OH], 209 [M^+-OBn], 195 [M^+-OBz], 91 (100), 77 (53).

(2S)-3-Benzoyloxy-4-benzyloxy-1-butene (5) :

Methods A and B were used to eliminate **4** (290 mg, 0.91 mmol) yielding, after chromatography, **5** (233 mg, 0.82 mmol, 90%, method A), (154 mg, 0.54 mmol, 60%, method B): $[\alpha]_D^{25}$ −12.5 (c 1.5, $CHCl_3$); ^1H NMR, δ: 3.73 (m, 2H), 4.62 (d, J=4.01Hz, 2H), 5.40 (m, 2H), 5.76 (m, 1H), 5.95 (m, 1H), 7.35 (m, 5H), 7.55 (m, 3H), 8.13 (m, 2H); ^{13}C NMR, δ: 71.16 (t), 73.57 (t), 73.61 (d), 118.47 (t), 128.13 (d), 128.84 (d), 130.17 (d), 133.46 (d), 133.79 (d), 138.39 (s), 166.50 (s); I.R. ($CHCl_3$) (cm^{-1}): 3500, 2974, 2865, 1716, 1602, 1452, 1272, 1212, 1111, 1026; MS *m/z* (rel. int.): 175 [M^+-OBn], 161 [M^+-OBz], 105 (100), 91 (50).

(2S, 3R)-3-Benzoyloxy-8-acetyloxy-1,2-octanediol (6) :

The general procedure to obtain 1,2-diol benzoates was used on (*E*)-8-acetyloxy-2-octen-1-ol (1.6 g, 11 mmol) yielding **6** (2.49 g, 7.7 mmol, 70%): $[\alpha]_D^{25}$ +27.7 (c 0.202, $CHCl_3$); ^1H NMR, δ: 1.34 (m, H), 1.58 (m, H), 1.97 (s, 3H), 3.72 (m, 3H), 3.99 (t, J=6.62 Hz, 2H), 5.09 (m, 1H), 7.51 (m, 4H), 7.98 (m, 2H); ^{13}C NMR, δ: 21.50 (q), 25.06 (t), 25.73 (t), 29.40 (t), 30.68 (t), 62.42 (t), 64.33 (t), 72.99 (d), 74.65 (d), 129.53 (d), 129.75 (d), 133.49 (d); I.R. ($CHCl_3$) (cm^{-1}): 3567, 2830, 2357, 1683, 1634, 1457, 1362, 1320, 1093, 987, 895; MS *m/z* (rel. int.): 307 [M^+-OH], 105 (100), 99 (17), 77 (32).

(3R)-3-Benzoyloxy-8-acetyloxy-1-octene (7) :

Methods A and B were used to eliminate **6** (450 mg, 1.22 mmol and 380 mg, 1.03 mmol, respectively) yielding, after chromatography **7** (290 mg, 1 mmol, 82%, method A) (182 mg, 0.62 mmol, 61%, method B): $[\alpha]_D^{25}$ −17.4 (c 0.2, $CHCl_3$); ^1H NMR, δ: 1.49 (m, 4H), 1.67 (m, 4H), 2.03 (s, 3H), 4.05 (t, J=6.54 Hz, 2H), 5.24 (m, 2H), 5.47 (m, 1H), 5.86 (m, 1H), 7.46 (m, 3H), 8.08 (m, 2H); ^{13}C NMR, δ: 24.73 (q), 25.75 (t), 28.46 (t), 29.68 (t), 30.30 (t), 34.17 (t), 64.36 (t), 75.10 (d), 116.73 (t), 128.34 (d), 129.56 (d), 132.66 (d), 136.42 (d); I.R.(cm^{-1}) ($CHCl_3$): 3025, 2927, 2857, 1716, 1601, 1451, 1273, 1208, 1114; MS *m/z* (rel. int.): 290 [M^+], 231 [M^+-OAc], 105 (100), 64 (35).

(2S,3R)-3-Benzoyloxy-8-(2'-tetrahydropyranyl)oxy-1,2-octanediol (8) :

The general procedure to obtain 1,2-diol benzoates was used on (*E*)-8-(2'-tetrahydropyranyloxy)-2-octen-1-ol (1.6 g, 7 mmol) yielding **8** (1.82 g, 4.97 mmol, 80%): $[\alpha]_D^{25}$ +23.69 (c 1.11, $CHCl_3$); ^1H NMR, δ: 1.55 (m, 14H), 3.67 (m, 6H), 4.52 (s, 1H), 5.10 (m, 1H), 7.43 (m, 3H), 7.99 (m, 2H); ^{13}C NMR, δ: 19.54 (t), 25.14 (t), 25.34 (t), 26.02 (t), 29.42 (t), 30.54 (t), 30.61 t), 62.26 (t), 62.55 (t), 67.35 (t), 72.98 (d), 74.60 (d), 98.78 (d), 128.38 (d), 129.65 (d), 133.25 (d); I.R. ($CHCl_3$) (cm^{-1}): 3463, 2944, 2862, 1070, 1061, 1354, 1282, 1118, 1072, 1035, 985; MS *m/z* (rel. int.): 367 [M^++1], 265 [M^+-OTHP], 105 (64), 85 (100), 55 (22).

(3R)-3-Benzoyloxy-1-octene-8-ol (9) :

Method A was used to eliminate **8** (0.254 mg, 0.6 mmol) yielding, after chromatography **9** (137 mg, 0.5 mmol, 80%): $[\alpha]_D^{25}$ -18.2 (c 1.7, $CHCl_3$); ^1H NMR, δ: 1.67 (m, 8H), 3.63 (t, J=6.48 Hz, 2H), 5.22 (m, 1H), 5.35 (m, 1H), 5.49 (m, 1H), 5.89 (m, 1H), 7.50 (m, 3H), 8.05 (m, 2H). ^{13}C RMN, δ: 32.85 (t), 45.31 (t), 63.18 (t), 64.26 (t), 75.58 (d), 117.18 (t), 128.77 (d), 129.99 (d), 133.32 (d), 136.93 (d), 161.53 (s); I.R. ($CHCl_3$) (cm^{-1}): 3450, 3000, 2870, 1720, 1620, 1490, 1455, 1320, 1275, 1120, 1030, 935. MS: 231 [M^+-OH], 127 [M^+-OBz], 105 (100), 76 (72), 67 (31).

(3R)-3-Benzoyloxy-8-(2'-tetrahydropiranyl)oxy-1-octene (10) :

Method B was used to eliminate **8** (428 mg, 1.17 mmol) yielding, after chromatography **10** (205 mg, 0.62 mmol, 53%): $[\alpha]_D^{25}$ −17.3 (c 1.0, $CHCl_3$); ^1H NMR, δ: 1.62 (m, 14H), 3.40 (m, 1H), 3.49 (m, 1H), 3.78 (m, 1H), 3.90 (m, 1H), 4.60 (s, 1H), 5.24 (d, J=10.52 Hz, 1H), 5.36 (m, 1H), 5.55 (m, 1H), 6.00 (m, 1H), 7.49 (m, 3H), 8.11 (m, 2H); ^{13}C NMR, δ: 19.63 (t), 24.93 (t), 25.45 (t), 26.08 (t), 29.58 (t), 30.72 (t), 34.24 (t), 62.27 (t), 67.39 (t), 75.22 (d), 98.60 (d), 116.56 (t), 128.29 (d), 129.54 (d), 132.60 (d), 136.53 (d); I.R. ($CHCl_3$) (cm^{-1}): 2943, 2859, 1712, 1649, 1274, 1117, 1071, 989; MS *m/z* (rel. int.): 333 [M^++1], 303 [M^+-C_2H_3], 231 [M^+-OTHP], 85 (100), 67 (42).

(2S,3R)-3-Benzoyloxy-8-*tert*-butyldimethylsilyloxy-1,2-octanediol (11) :

The general procedure to obtain 1,2-diol benzoates was used on (*E*)-8-*tert*-butyldimethylsilyloxy-2-octen-1-ol (1.8 g, 6.9 mmol) yielding **11** (1.74 g, 4.83 mmol, 70%): $[\alpha]_D^{25}$ +19.51 (c 1.62, $CHCl_3$); ^1H NMR, δ: 0.87 (s, 15H), 1.45 (m, 6H), 1.84 (m, 2H), 3.68 (m, 2H), 5.09 (m, 1H), 7.47 (m, 4H), 8.06 (m, 2H); ^{13}C NMR, δ: 25.28 (t), 25.64 (t), 25.93 (s), 62.44 (t), 63.02 (t), 73.07 (d), 74.93 (d), 128.5 (d), 129.77 (d), 130.1 (d), 133.43 (d). I.R. ($CHCl_3$) (cm^{-1}): 3542, 2930, 2857, 1702, 1270, 1097, 967, 837; MS *m/z* (rel. int.): 379 [M^+-OH], 339 [M^+-*t*-Bu], 105 (100), 75 (51), 57 (11).

(3R)-3-Benzoyloxy-8-*tert*-butyldimethylsilyloxy-1-octene (12) :

Method B was used to eliminate **11** (300 mg, 0.75 mmol) yielding, after chromatography, **12** (181 mg, 66%): $[\alpha]_D^{25}$ −14.0 (c 1.2, $CHCl_3$); ^1H NMR, δ: 0.89 (s, 15H), 1.44 (m, 6H), 1.78 (m, 2H), 3.60 (t, J=6.32 Hz, 2H), 5.28 (m, 2H), 5.50 (m, 1H), 5.90 (m, 1H), 7.53 (m, 3H), 8.09 (m, 2H); ^{13}C NMR, δ: 24.77 (t), 25.52 (t), 25.82 (s), 32.54 (t), 34.22 (t), 62.90 (t), 75.15 (d), 116.44 (t), 128.17 (d), 129.43 (d), 132.66 (d), 136.44 (d); I.R. ($CHCl_3$) (cm^{-1}): 3032, 3015, 2923, 1842, 1454, 1218, 1099, 737; MS *m/z* (rel. int.): 305 [M^+-tBu], 179

(100), 105 (69), 57 (9).

(2S, 3R)-3-Benzoyloxy- 5-*tert*-butyldiphenylsilyloxy-1,2-pentanediol (13):

The general procedure to obtain 1,2-diol benzoates was used on (*E*)-5-*tert*-butyldiphenylsilyloxy-2-penten-1-ol (1.5 g, 4.4 mmol) yielding, after chromatography, **13** (1.57 g, 3.52 mmol, 80%): $[\alpha]_D^{25}$ +10.79 (c 3.52, $CHCl_3$); ^1H NMR, δ: 1.05 (s, 9H), 2.13 (m, 2H), 3.63 (m, 5H), 5.34 (m, 1H), 7.34 (m, 5H), 7.55 (m, 3H), 7.98 (m, 2H); ^{13}C NMR, δ: 18.95(s), 26.67 (q), 33.37 (t), 59.64 (t), 62.77 (t), 72.12 (d), 73.00 (d), 127.67 (d), 128.36 (d), 129.61 (d), 133.04 (d), 135.44 (d), 166.50 (s); I.R.($CHCl_3$) (cm^{-1}): 3486, 2931, 2858, 1700, 1633, 1361, 1278, 1127, 997; MS *m/z* (rel. int.): 341 (21), 283 (100), 267 [M^+-Ph_2-*t*-Bu], 223 [M^+-Ph_2-*t*-BuSiO], 105 (62), 91 (72).

(3R)-3-Benzoyloxy-5-*tert*-butyldiphenylsilyloxy-1-pentene (14) :

Methods A and B were used to eliminate **13** (350 mg, 0.75 mmol) yielding, after chromatography **14** (67.81 mg, 0.165 mmol, 22%, method A), (194 mg, 0.47 mmol, 60% method B): $[\alpha]_D^{25}$ –7.3 (c 1.5, $CHCl_3$); ^1H NMR δ: 1.03 (s, 9H), 2.03 (m, 2H), 3.78 (t, J=6.01 Hz, 2H), 5.27 (m, 2H), 5.74 (m, 1H), 5.86 (m, 1H), 7.39 (m, 5H), 7.62 (m, 3H), 8.03 (m, 2H); ^{13}C NMR, δ: 18.74(s), 25.32 (q), 34.73 (t), 59.94 (t), 72.44 (d), 116.53 (d), 127.63 (d), 128.26 (d), 130.73 (d), 132.72 (d), 135.59 (d), 136.58 (d), 165.58 (s); I.R. ($CHCl_3$) (cm^{-1}): 2932, 2858, 1715 ,1651, 1361, 1315, 1274, 1111, 987, 895; MS *m/z* (rel. int.): 303 (43), 243 (30), 105 (100), 77 (67), 67 (38).

3-Benzoyloxy-1,2-cyclohexanediol (15) :

The general procedure to obtain 1,2-diol benzoates was used on 2-cyclohexen-1-ol (2 g, 20 mmol) yielding **15** (3.3 g, 14 mmol, 70%): ^1H NMR, δ: 1.61 (m, 3H), 1.66 (m, 1H), 1.81 (m, 1H), 2.14 (m, 1H), 3.81 (m, 1H), 4.17 (m, 1H), 5.30 (m, 1H), 7.46 (m, 2H), 7.61 (m, 1H), 8.09 (m, 1H); ^{13}C NMR, δ: 18.11 (t), 29.02 (t), 29.62 (t), 69.81 (d), 74.24 (d), 75.14 (d), 128.40 (d), 129.70 (d), 133.20 (d); I.R. ($CHCl_3$) (cm^{-1}): 3576, 3018, 2948, 1715, 1451, 1274, 1112, 1026, 999; MS *m/z* (rel. int.): 237 [M^++1], 219 [M^+-OH], 115 [M^+-OBz], 114 (3), 104 (100).

3-Benzoylcyclohexene (16) :

Method B was used to eliminate **15** (380 mg, 1.61 mmol) yielding, after chromatography **16** (195 mg, 0.96 mmol, 60%): ^1H NMR, δ:1.79 (m, 6H), 5.42 (m, 1H), 5.77 (m, 1H), 5.90 (m, 1H), 7.40 (m, 1H), 7.95 (m, 2H); ^{13}C NMR, δ: 18.92(t), 24.93 (t), 28.40 (t), 68.56 (d), 125.72 (d), 127.72 (d), 129.56 (d), 132.71 (d); I.R. ($CHCl_3$) (cm^{-1}): 2947, 2833, 1708, 1615, 1337, 1273, 1116, 1007, 914; MS *m/z* (rel. int.): 202 [M^+], 105 (100), 81 [M^+-OBz], 77 (74), 51 (42).

(R)-1-Hexen-3-ol :

To a freshly prepared solution of sodium methoxide in dry CH_2Cl_2 (50 mL) [made by adding dry MeOH (0.8 mL) to a suspension of NaH, 320 mg (10.5 mmol) of 80% dispersion in mineral oil] was added **2** (1.98 g, 9.7 mmol). The reaction was completed in five minutes. The reaction mixture was transferred to a separatory funnel and washed with brine (2 x 20 mL), dried, filtered, concentrated and purified by column chromatography, yielding (R)-1-hexen-3-ol (922 mg, z mmol, 95%): $[\alpha]_D^{25}$ -11.5 (c 0.56, $CHCl_3$); ^1H RMN δ: 0.93 (t, J=7.2 Hz, 3H), 1.39 (m, 4H), 4.11 (m, 1H), 5.08 (m, 1H), 5.19 (m, 1H), 5.86 (m, 1H); ^{13}C RMN δ: 14.40 (q), 18.90 (t), 39.54 (t), 73.39 (d), 114.85 (t), 141.76 (d); I.R. ($CHCl_3$) (cm^{-1}): 3460, 2910, 1735, 1655, 1615, 1445, 1400, 1305, 1210, 1135, 1120, 950; MS *m/z* (rel. int.): 100 [M^+], 83 [M^+-OH], 57 (100), 43 (72).

(2R, 3R)-1,2-Epoxy-3-hexanol (17) :

Powdered, activated molecular sieves (4Å, 0.1g) were added to stirred CH_2Cl_2 (35 ml). The flask was cooled to -20 °C and $Ti(OPr\text{-}i)_4$ (0.094 ml, 0.3 mmol), L-(+)-DET (0.075 ml, 0.36 mmol), and (R)-1-hexen-3-ol (524 mg, 5.23 mmol) were added sequentially with stirring. The reaction mixture was stirred for 20 min and TBHP (1.55 ml, 5.7 M in *iso*-octane, 6.2 mmol) was added slowly. After the addition, the reaction was maintained with stirring for 3 h. Tartaric acid aqueous solution (15%, 20 mL) was added and the stirring continued until clear phases were reached (30 min). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 25 mL). The combined organic phases were washed with brine (25 mL), dried, evaporated and purified by column chromatography to yield **17** (474 mg, 9.22 mmol, 78% yield): $[\alpha]_D^{25}$ -24.4 (c 1.03, $CHCl_3$); ^1H NMR, δ: 0.93 (m, 3H), 1.44 (m, 4H), 2.70 (m, 1H), 2.72 (m, 1H), 3.01 (m, 1H), 3.84 (m, 1H); ^{13}C RMN,

δ: 14.44 (q), 18.91 (t), 36.11 (t), 45.55 (t), 68.60 (d), 71.87 (d); I.R. ($CHCl_3$) (cm^{-1}): 3500, 2995, 1610, 1470, 1385, 1230, 1140, 1070, 985; MS *m/z* (rel. int.): 117 [M^++1], 116 [M^+], 99 [M^+-OH], 73 (46), 55 (100), 43 (55).

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