Concise Synthesis of Optically Pure *syn*-1,3-Diols by Stereoselective Desymmetrization of a Divinylcarbinol

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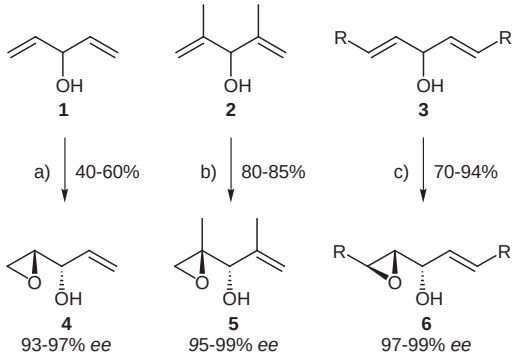
Abstract: Divinylcarbinols **17** and **18**, *C*S-symmetrical and *cis*-configured, were desymmetrized by Sharpless' asymmetric epoxidation. This furnished *anti*-configured monoepoxy alcohols **19** (85% ee) and **20** (94% ee), respectively, or their mirror images (*ent*-**19**, 84% ee; *ent*-**20**, 95% ee). **20** (*ent*-**20**) was reduced by Red-Al® regio- and chemoselectively, providing *syn*-1,3-diols *ent*-**21** (**21**) at low and *ent*-**22** (**22**) at higher temperature (94–95% ee). They should allow the obtention of more elaborated *syn*-1,3-diols.

Key words: acetonides, desymmetrization, 1,3-diols, epoxyalcohols, Sharpless asymmetric epoxidation

The asymmetric desymmetrization of prochiral molecules with or without stereocenters (i. e., *meso* compounds) is an efficient means for generating multifunctional compounds enantioselectively,[1,2] one advantage being that, in principle, the underlying substrates can emerge from highly efficient 'bidirectional synthetic strategies'.[3] In this context the asymmetric desymmetrization of divinylcarbinol and derivatives thereof by Sharpless' asymmetric epoxidation[4] (SAE) received considerable attention. This process was examined with divinylcarbinol (**1**),[5] with its methallyl analog **2**,[5c,6] and with *trans*-configured dialkenylcarbinols **3**[7] (Scheme 1). Several of the resulting epoxy alcohols **4**–**6** were obtained with exceptionally high *ee* values: up to 99%. This was explained by Schreiber et al.[5c] based upon formal kinetics; the crucial point being that in these cases the initial asymmetric epoxidation is followed by an ee-enhancing kinetic resolution through a second epoxidation.

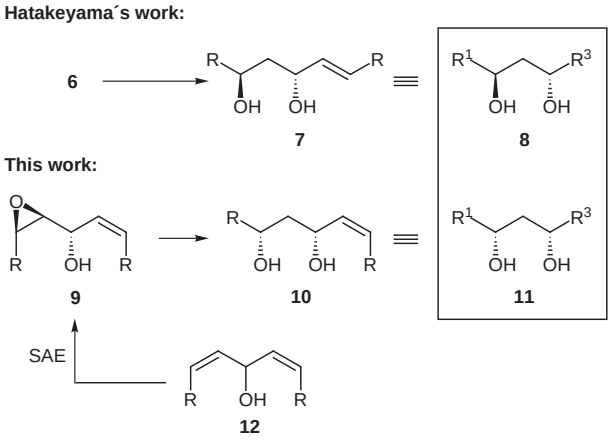
Epoxy alcohols **4** and **5** (Scheme 1) were employed as enantiomerically pure building blocks in the synthesis of polyhydroxylated natural products such as sugars or polyol macrolide antibiotics,[5,6] while type-**6** epoxy alcohols have not seen many synthetic applications yet. They are amenable, though, to the stereocontrolled synthesis of *anti*-configured 1,3-diols through a regioselective ring-opening of the epoxide ring by a hydride nucleophile as shown by Hatakeyama et al.[7b–d]: epoxy alcohols **6** and Red-Al® give 1,3-diols **7** (Scheme 2, top).

The latter compounds exhibit the *anti*-1,3-diol motif **8**. It abounds in polyol, polyene macrolide antibiotics, a class



Scheme 1 Previous desymmetrizations of divinylcarbinols by Sharpless' asymmetric epoxidation. a) Ref.[5]; b) ref.[6]; c) ref.[7]

of compounds well beyond 200 members.[8a] There, however, motif **8** is always intermingled with the diastereomorphic motif **11** exhibiting the *syn*-configuration. Considering this and the persistent need for methods tailored for the synthesis of such macrolides[8] we investigated the reaction sequence outlined in Scheme 2 below Hatakeyama's work. It is stereochemically complementary to his method and starts from a *cis*-configured type-**12** divinylcarbinol. Enantio- and diastereoselective desymmetrizations by SAE were meant to furnish type-**9** epoxy alcohols and their reductions to lead to *syn*-1,3-diols **10**. These diols are versatile examples of type-**11** diols.



Scheme 2 Divinylcarbinol → epoxy alcohol → 1,3-diol strategies.

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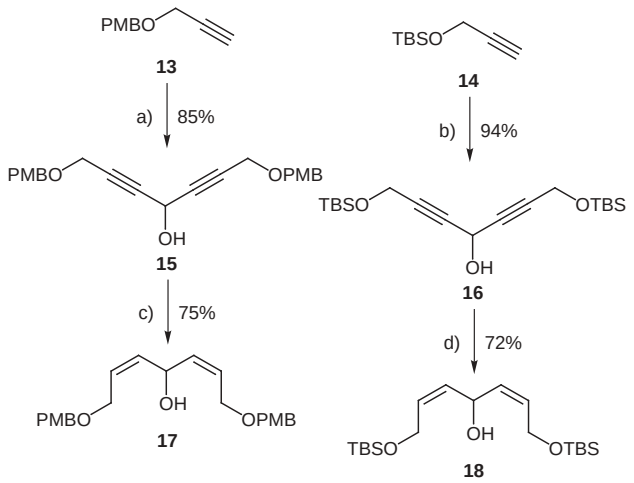
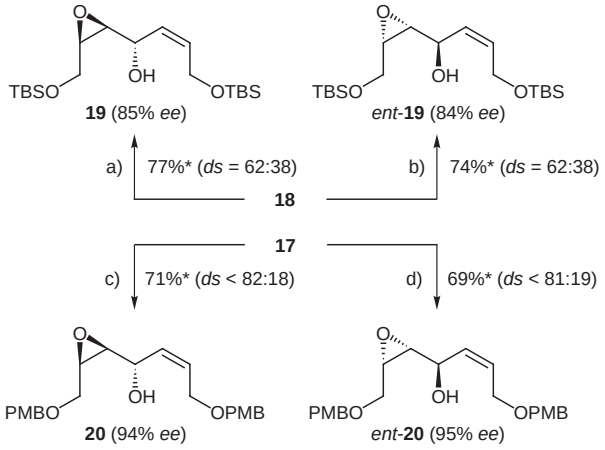


Scheme 3 a) **13** (2.3 equiv), *n*-BuLi (2.1 equiv), THF, –78 °C, 70 min, addition of HCO_2Et, → –35 °C in 20 h; b) **14** (2.03 equiv), *n*-BuLi (2.03 equiv), THF, –78 °C, 40 min, addition of HCO_2Et, → –30°C in 15 h; c) $ZnCl_2$ (14 equiv), K (27 equiv), THF, reflux, 4.5 h, addition of **15** in MeOH, 40 min; d) $ZnCl_2$ (13 equiv), K (25 equiv), THF, reflux, 3 h, addition of **16** in MeOH, 10 min, addition of H_2O, 5 h.



Scheme 4 a) Molecular sieves 4 Å, Ti(O*i*-Pr)$_4$ (1.0 equiv), L-(+)-diisopropyltartrate (1.1 equiv), CH_2Cl_2, –25 °C, 50 min, addition of **18**, 1 h; addition of *t*-BuOOH (1.4 equiv), 5 d, addition of *t*-BuOOH (0.65 equiv), 17 h; b) Same as (a) with D-(–)-diisopropyltartrate; c) Molecular sieves 4 Å, Ti(O*i*-Pr)$_4$ (1.0 equiv), L-(+)-diisopropyltartrate (1.1 equiv), CH_2Cl_2, –25 °C, 1 h, addition of **17**, 20 min, addition of *t*-BuOOH (1.4 equiv), 2 d, addition of *t*-BuOOH (0.3 equiv), 18 h; d) Molecular sieves 4 Å, Ti(O*i*-Pr)$_4$ (1.0 equiv), D-(–)-diisopropyltartrate (1.1 equiv), CH_2Cl_2, –25 °C, 1 h, addition of **17**, 70 min, addition of *t*-BuOOH (1.4 equiv), 55 d, addition of *t*-BuOOH (0.7 equiv), 2 d. *Yield based on re-isolated starting material.

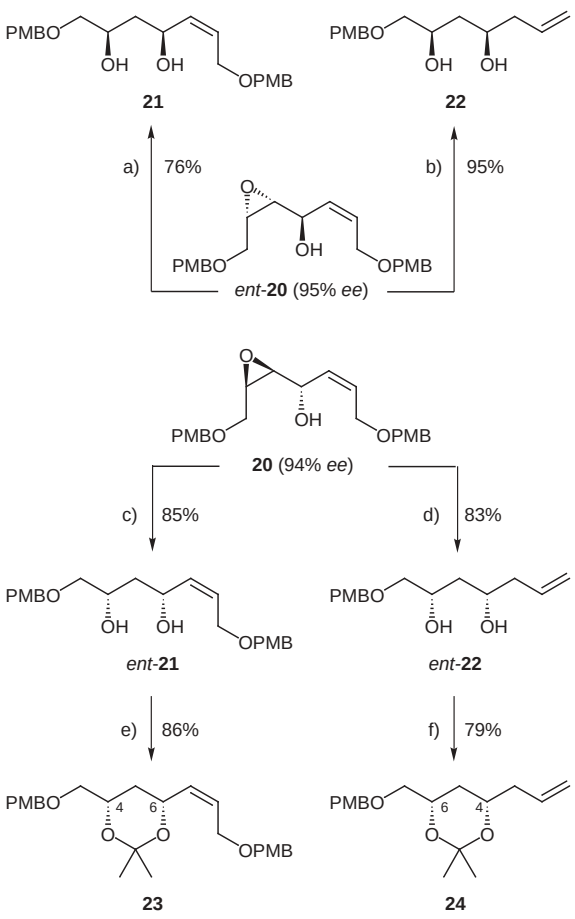
To the best of our knowledge, our preparation of the *cis*-configured type-**12** divinylcarbinols **17** and **18** is unprecedented (Scheme 3). Firstly propargyl ethers **13** and **14** were deprotonated giving the corresponding acetylide anion. Then 0.5 equivalent of ethyl formate were added. This furnished dialkynylcarbinols **15** (85%) and **16**[9] (94%), respectively.[10] Their hydrogenation in the presence of Lindlar's catalyst gave complex mixtures. Therefore, we chose Rieke zinc[11] in methanol as the reducing agent.[12] We obtained the desired divinylcarbinols **17** and **18** as pure stereoisomers in 75% and 72% yield, respectively. Their assignments as *cis*-olefins are in accordance with vicinal olefinic $^1H,^1H$ coupling constants of 11.2 Hz and 11.3 Hz, respectively.

We were aware that SAEs of *cis*-configured (primary) allyl alcohols normally proceed with diminished enantioselectivity compared to their *trans*-isomers.[13] In agreement with this, SAEs of *cis*-2-butene-1,4-diol mono-protected with the *t*-BuMe_2Si- or the PMB group, i. e., of (primary) vinyl carbinols analogous to our (secondary) divinylcarbinols **17** and **18**, are reported to yield epoxy alcohols with no more than 84–85%[14] and 85–88% ee,[15] respectively. Still, we hoped for a higher level of enantioselectivity in the SAEs of **17** and **18** because of the expected kinetic resolution taking place after the initial epoxidation of the unsubstituted and *trans*-substituted divinylcarbinols **1**–**3** discussed in Scheme 1.

SAEs of the *t*-BuMe_2Si-protected divinylcarbinol **18** with stoichiometric amounts of Ti(*i*-PrO)$_4$ and L-(+)-diisopropyltartrate (→ **19**) or D-(–)-diisopropyltartrate (→ *ent*-**19**) suffered from low diastereoselectivities (ds = 62:38)[16] and moderate enantiopurities of the major diastereomer (ee = 84–85%; determined by HPLC, Scheme 4). The combined yields of the two diastereomeric monoepoxyalcohols obtained as a mixture after standard flash chromatography on silica gel[17] were 77% and 74%, respectively. Separation of pure major diastereomer by the same technique was tedious. It delivered 39% **19** in one optical series and 19% *ent*-**19** in the other (already taking into account that 14–17% of unreacted divinylcarbinol **18** were recovered).

Success came during desymmetrizing of the PMB-protected divinylcarbinol **17** (Scheme 4): Exposure to stoichiometric amounts of L-(+)- or D-(–)-diisopropyltartrate containing SAE cocktails furnished epoxy alcohols **20** and *ent*-**20** in yields of 71% and 69%, respectively (taking into account 5–8% recovered unreacted **17**).[18] Increased values of diastereo- (ds < 81:19)[19] and enantioselectivity (ee = 94–95% in the major diastereomer; determined by HPLC) were observed compared to the previous desymmetrization. Repeated flash chromatography on silica gel[17] provided the main diastereomers pure: 27% **20**[20] and 22% *ent*-**20**, respectively.

The somewhat easier purification made us continue the route towards *syn*-1,3-diol building blocks with the PMB-protected epoxyalcohols **20** (94% *ee*) and *ent*-**20** (95% *ee*) rather than with their *t*-BuMe_2Si-protected analogs[21] **19** and *ent*-**19** using Hatakeyama's protocol[7c] (Scheme 5). Treatment of **20** with Red-Al® (10 equiv) in toluene at –40 °C gave *syn*-1,3-diol, *ent*-**21**[22] in 85% yield.[23] Likewise, *ent*-**20** delivered **21** (76%). On the other hand, reduction of **20** and *ent*-**20** with Red-Al® (4 equiv) in toluene (or THF) at 60 °C proceeded beyond *ent*-**21** and **21**. It also brought about the loss of the PMBO group by an S_N2' substitution, thereby giving diols **22**[24] (95% yield) and *ent*-**22** (83% yield) as the only products, respectively.



Scheme 5 a) Red-Al® (10 equiv), toluene, –40 °C, 5 h; b) Red-Al® (4 equiv), THF, 60 °C, 2 h; c) Red-Al® (10 equiv), toluene, –40 °C, 6 h; d) Red-Al® (4 equiv), toluene, 60 °C, 2 h; e) 2,2-dimethoxypropane (6 equiv), pyridinium *p*-toluenesulfonate (4 mol%), acetone, 10 °C, 16 h; f) same as (e).

In order to elucidate the relative configuration of the OH groups in 1,3-diols *ent*-**21** and *ent*-**22**, these compounds were transformed into the corresponding acetonides **23** and **24** (Scheme 5; 86% and 79% yield, respectively). Their stereostructure is *cis* as concluded from the two Rychnovsky/Evans criteria for the ^{13}C NMR resonances of the protecting group of *cis*-4,6-disubstituted acetonides.[25] On the one hand, the $^{13}C_{quat}Me_2$ signals appear at δ = 19.69/30.13 (**23**) and 19.76/30.11 (**24**); this matches the typical δ values of 19.66 ± 0.35 and 30.00 ± 0.30. On the other hand, the $^{13}C_{quat}Me_2$ resonances are δ = 98.69 (**23**) and 98.62 (**24**) and thus within the standard range of δ = 98.93 ± 0.67.

In summary, we have synthesized enantiopure *syn*-1,3-diol building blocks, compounds **21**, **22**, and their enantiomers, from inexpensive propargyl alcohol in only 5 steps. As a key step we have desymmetrized a *cis*-configured dialkenylcarbinol by a SAE, which had not been studied previously for that kind of substrate.[26]

Acknowledgment

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References

(1) For leading references on asymmetric desymmetrizations of substrates containing no stereocenter, see: (a) Tamao, K.; Tohma, T.; Inui, N.; Nakayama, O.; Ito, Y. *Tetrahedron Lett.* **1990**, *31*, 7333. (b) Shibasaki, M.; Boden, C. D. J.; Kojima, A. *Tetrahedron* **1997**, *53*, 7371. (c) Angelaud, R.; Babot, O.; Charvat, T.; Landais, Y. *J. Org. Chem.* **1999**, *64*, 9613. (d) Bahmanyar, S.; Houk, K. N. *J. Am. Chem. Soc.* **2001**, *123*, 11273. (e) Evans, P. A.; Cui, J.; Buffone, G. P. *Angew. Chem. Int. Ed.* **2003**, *42*, 1734; *Angew. Chem*. **2003**, *115*, 1776.

(2) For leading references on asymmetric desymmetrizations of substrates, which are *meso*-configured, see: (a) Hodgson, D. M.; Gibbs, A. R.; Lee, G. P. *Tetrahedron* **1996**, *52*, 14361. (b) La, D. S.; Alexander, J. B.; Cefalo, D. R.; Graf, D. D.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **1998**, *120*, 9720. (c) Jacobsen, E. N. *Acc. Chem. Res.* **2000**, *33*, 421. (d) BouzBouz, S.; Cossy, J. *Org. Lett.* **2001**, *3*, 3995. (e) Katsuki, T. *Curr. Org. Chem.* **2001**, *5*, 663. (f) Harada, T.; Egusa, T.; Igarashi, Y.; Kinugasa, M.; Oku, A. *J. Org. Chem.* **2002**, *67*, 7080. (g) Vares, L.; Rein, T. *J. Org. Chem.* **2002**, *67*, 7226.

(3) (a) Schreiber, S. L. *Chem. Scr.* **1987**, *27*, 563. (b) Ward, R. S. *Chem. Soc. Rev.* **1990**, *19*, 1. (c) Poss, C. S.; Schreiber, S. L. *Acc. Chem. Res.* **1994**, *27*, 9. (d) Maier, M. In *Organic Synthesis Highlights II*; Waldmann, H., Ed.; VCH: Weinheim New York, **1995**, 203. (e) Magnuson, S. R. *Tetrahedron* **1995**, *51*, 2167. (f) Willis, M. C. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1765. (g) Hoffmann, R. W. *Angew. Chem. Int. Ed.* **2003**, *42*, 1096; *Angew. Chem.* **2003**, *115*, 1128.

(4) (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5976. (b) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.

(5) (a) Hatakeyama, S.; Sakurai, K.; Takano, S. *J. Chem. Soc., Chem. Commun.* **1985**, 1759. (b) Häfele, B.; Schröter, D.; Jäger, V. *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 87; *Angew. Chem.* **1986**, *98*, 89. (c) Schreiber, S. L.; Schreiber, T. S.; Smith, D. B. *J. Am. Chem. Soc.* **1987**, *109*, 1525. (d) Smith, D. B.; Wang, Z.; Schreiber, S. L. *Tetrahedron* **1990**, *46*, 4793. (e) Nakatsuka, M.; Ragan, J. A.; Sammakia, T.; Smith, D. B.; Uehling, D. E.; Schreiber, S. L. *J. Am. Chem. Soc.* **1990**, *112*, 5583. (f) Jäger, V.; Hümmer, W.; Stahl, U.; Gracza, T. *Synthesis* **1991**, 769.

(6) Hatakeyama, S.; Sakurai, K.; Numata, H.; Ochi, N.; Takano, S. *J. Am. Chem. Soc.* **1988**, *110*, 5201.

(7) (a) Herunsalee, A.; Isobe, M.; Pikul, S.; Goto, T. *Synlett* **1991**, 199. (b) Hatakeyama, S.; Satoh, K.; Takano, S. *Tetrahedron Lett.* **1993**, *34*, 7425. (c) Esumi, T.; Fukuyama, H.; Oribe, R.; Kawazoe, K.; Iwabuchi, Y.; Irie, H.; Hatakeyama, S. *Tetrahedron Lett.* **1997**, *38*, 4823. (d) Nishioka, T.; Iwabuchi, Y.; Irie, H.; Hatakeyama, S. *Tetrahedron Lett.* **1998**, *39*, 5597.

(8) (a) Omura, S.; Tanaka, H. In *Macrolide Antibiotics: Chemistry, Biology and Practice*; Omura, S., Ed.; Academic Press: New York, **1984**, 351–404. (b) Oishi, T.; Nakata, T. *Synthesis* **1990**, 635. (c) Rychnovsky, S. D. *Chem. Rev.* **1995**, *95*, 2021. (d) Schneider, C. *Angew. Chem. Int. Ed.* **1998**, *37*, 1375; *Angew. Chem.* **1998**, *110*, 1445.

(9) Compound **16** has been previously prepared, see ref.[7a]
(10) Except for compound **24**, all new compounds gave satisfactory ^{1}H NMR and IR spectra as well as correct combustion analyses.
(11) (a) Rieke, R. D.; Uhm, S. J.; Hudnall, P. M. *J. Chem. Soc., Chem. Commun.* **1973**, 269. (b) Rieke, R. D.; Uhm, S. J. *Synthesis* **1975**, 452.
(12) Procedure: (a) Avignon-Tropis, M.; Pougny, J. R. *Tetrahedron Lett.* **1989**, *30*, 4951. (b) Chou, W.-N.; Clark, D. L.; White, J. B. *Tetrahedron Lett.* **1991**, *32*, 299.
(13) (a) Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*; Ojima, I. E., Ed.; Wiley-VCH: New York, **1993**, 103–158. (b) Katsuki, T.; Martin, V. S. *Org. React.* **1996**, *48*, 1.
(14) SAEs of *cis*-2-butene-1,4-diol mono-protected with a *tert*-butyldimethylsilyl roup: (a) Astles, P. C.; Thomas, E. J. *J. Chem. Soc., Perkin Trans. 1* **1997**, 845; 85% ee. (b) Shibuya, H.; Kawashima, K.; Narita, N.; Ikeda, M.; Kitagawa, I. *Chem. Pharm. Bull.* **1992**, *40*, 1154; 84–85% ee.
(15) SAEs of *cis*-2-butene-1,4-diol mono-protected with a PMB group: (a) Williams, R. M.; Rollins, S. B.; Judd, T. C. *Tetrahedron* **2000**, *56*, 521; 88% ee. (b) Yoshino, T.; Nagata, Y.; Itoh, E.; Hashimoto, M.; Katoh, T.; Terashima, S. *Tetrahedron* **1997**, *53*, 10239; 85% ee.
(16) This was concluded from the integral ratio of the peaks attributed to 3-H [δ_{major} = 3.02 (dd; **19**/*ent*-**19**), δ_{minor} = 3.08(dd)].
(17) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(18) In addition, we retrieved inseparable mixtures of mono- with bis-epoxides.
(19) This was concluded from the integral ratio of the peaks attributed to 3-H [δ_{major} = 3.00 (dd; **20**/*ent*-**20**), δ_{minor} = 3.06(dd)].
(20) *cis*-(2*R*,3*S*,4*S*)-2,3-Epoxy-1,7-bis-[4-methoxybenzyl)oxy]-5-hepten-4-ol(**20**): $[\alpha]_D^{25}$ = –30.9 (*c* = 0.58 in $CHCl_3$); – 94.4% ee by HPLC.
^{1}H NMR (500.0 MHz, $CDCl_3$): δ = 2.80 (d, $J_{OH,4}$ = 2.3 Hz, OH), 3.00 (dd, $J_{3,4}$ = 7.5 Hz, $J_{3,2}$ = 4.3 Hz, 3-H), 3.25 (m_c, probably incompletely resolved ddd: $J_{2,1\text{-}H(A)} = J_{2,1\text{-}H(B)}$ = ca. 5.7 Hz, $J_{2,3}$ = 4.3 Hz, 2-H), AB signal (δ_A = 3.63, δ_B = 3.79, J_{AB} = 11.1 Hz, in addition split by $J_{A,2}$ = 6.2 Hz, $J_{B,2}$ = 5.4 Hz, 1-H_2), B part superimposed by 3.80 (s, 2 × OCH_3), AB signal (δ_A = 4.05, δ_B = 4.11, J_{AB} = 12.9 Hz, in addition split by $J_{A,6}$ = 5.7 Hz, $^4J_{A,5\text{-}H}$ = 1.4 Hz, $J_{B,6}$ = 6.7 Hz, $^4J_{B,5\text{-}H}$ = 1.5 Hz, 7-H_2), 4.25 (br dd, $J_{4,3} = J_{4,5}$ = 7.5 Hz, 4-H), 4.42 (s, 1′′-H_2)*, AB signal (δ_A = 4.46, δ_B = 4.54, J_{AB} = 11.4 Hz, 1′-H_2), 5.70 (dddd, J_{cis} = 11.3 Hz, $J_{5,4}$ = 7.6 Hz, $^4J_{5,7\text{-}H(A)} = {}^4J_{5,7\text{-}H(B)}$ = 1.5 Hz, 5-H), 5.82 (br ddd, J_{cis} = 11.4 Hz, $J_{6,7\text{-}H(A)} = J_{6,7\text{-}H(B)}$ = 6.0 Hz, 6-H), AA′BB′ signal centered at δ = 6.88 and δ = 7.26 (2 × C_6H_4).
^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 54.73 (C-2), 55.26 (2 × O*C*H_3), 58.12 (C-3), 65.80 (C-7), 66.34 (C-4), 68.00 (C-1), 72.02 (C-1′′), 73.20 (C-1′), 113.83, 113.96, 129.46, and 129.60 (2 × 2 × C_{ortho}, 2 × 2 × C_{meta}), 129.32, 130.03, 159.28, and 159.51 (2 × C_{para}, 2 × C_{ipso}), 130.29 (C-6), 131.71 (C-5).
IR(film): 3400, 3000, 2935, 2910, 2860, 2835, 1610, 1585, 1515, 1460, 1300, 1250, 1175, 1075, 1035, 850, 820 cm^{-1}.
Anal. Calcd for $C_{23}H_{28}O_6$ (400.5): C, 68.98; H, 7.05. Found C, 68.99; H, 7.20.
(21) Moreover, *tert*-butyldimethylsiloxy groups do not withstand prolonged exposure to Red-Al®: Berkenbusch, T. *PhD Dissertation*; Universität Freiburg: Germany, **2002**.
(22) *cis*-(2*S*,4*R*)-1,7-Bis-[(4-methoxybenzyl)oxy]-5-heptene-2,4-diol (*ent*-**21**): $[\alpha]_D^{25}$ = 14.8 (*c* = 0.78 in $CHCl_3$).
^{1}H NMR (500.0 MHz, $CDCl_3$): δ = AB signal (δ_A = 1.55, δ_B = 1.71, J_{AB} = 14.2 Hz, in addition split by $J_{A,4}$ = 4.4 Hz, $J_{A,2}$ = 2.7 Hz, $J_{B,2}$ = 9.9 Hz, $J_{B,4}$ = 8.8 Hz, 3-H_2), 3.07 (br s, 2 × OH), AB signal (δ_A = 3.35, δ_B = 3.40, J_{AB} = 9.5 Hz, in addition split by $J_{A,2}$ = 7.1 Hz, $J_{B,2}$ = 4.1 Hz, 1-H_2), 3.795 and 3.804 (2 × s, 2 × OCH_3), 3.96 (m_c, 2-H), AB signal (δ_A = 4.06, δ_B = 4.09, J_{AB} = 12.4 Hz, in addition split by $J_{A,6}$ = 6.1 Hz, $^4J_{A,5\text{-}H}$ = 1.3 Hz, $J_{B,6}$ = 6.4 Hz, $J_{B,5\text{-}H}$ = 1.3 Hz, 7-H_2), AB signal (δ_A = 4.43, δ_B = 4.46, J_{AB} = 11.2 Hz, 1′-H_2), B part partly superimposed by 4.47 (s, 1′′-H_2), 4.67 (ddd with incompletely resolved allylic couplings, $J_{4,5} = J_{4,3\text{-}H(B)}$ = 8.4 Hz, $J_{4,3\text{-}H(A)}$ = 4.2 Hz, 4-H), 5.60 (dddd, J_{cis} = 11.4 Hz, $J_{5,4}$ = 8.0 Hz, $^4J_{5,7\text{-}H(A)} = {}^4J_{5,7\text{-}H(B)}$ = 1.3 Hz, 5-H), 5.68 (dddd, J_{cis} = 11.2 Hz, $J_{6,7\text{-}H(A)} = J_{6,7\text{-}H(B)}$ = 6.2 Hz, $^4J_{6,4}$ = 0.9 Hz, 6-H), AA′BB′ signal centered at δ = 6.87 and δ = 7.25 (2 × C_6H_4).
^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 39.74 (C-3), 55.26 (2 × OCH_3), 65.54, 67.63, 70.20, 72.19, 73.06 and 74.00 (C-1, C-2, C-4, C-7, C-1′, C-1′′), 113.85, 127.69, 129.40, 129.50, 129.93, 129.97, 135.72, 159.32, and 159.33 (9 resonances for 10 non-equivalent nuclei: C-5, C-6, 2 × C_6H_4).
IR(film): 3400, 3000, 2920, 2855, 1615, 1585, 1515, 1465, 1455, 1445, 1420, 1360, 1300, 1245, 1175, 1075, 1030, 820 cm^{-1}.
Anal. Calcd for $C_{23}H_{30}O_6$ (402.5): C, 68.64; H, 7.51. Found: C, 68.34; H, 7.24.
(23) Regioselective reductions of α,β-epoxy alcohols resulting in 1,3-diols (Red-Al®-method) or 1,2-diols (DIBAL-method): (a) Finan, J. M.; Kishi, Y. *Tetrahedron Lett.* **1982**, *23*, 2719. (b) Viti, S. M. *Tetrahedron Lett.* **1982**, *23*, 4541.
(24) (2*R*,4*R*)-1-[(4-Methoxybenzyl)oxy]-6-heptene-2,4-diol (**22**): $[\alpha]_D^{25}$ = –1.9 (*c* = 0.81 in $CHCl_3$).
^{1}H NMR (500.0 MHz, $CDCl_3$): δ = AB signal (δ_A = 1.53, δ_B = 1.62, J_{AB} = 14.4 Hz, in addition split by $J_{A,2} = J_{A,4}$ = 9.8 Hz, $J_{B,2} = J_{B,4}$ = 2.7 Hz, 3-H_2), 2.25 (dddd, $J_{5,6}$ = 7.3 Hz, $J_{5,4}$ = 6.2 Hz, $^4J_{5,7\text{-}H(E)} = {}^4J_{5,7\text{-}H(Z)}$ = 1.1 Hz, 5-H_2), 2.91–3.28 (m, 2 × OH), AB signal (δ_A = 3.35, δ_B = 3.43, J_{AB} = 9.4 Hz, in addition split by $J_{A,2}$ = 7.1 Hz, $J_{B,2}$ = 3.9 Hz, 1-H_2), 3.81 (s, OCH_3), 3.92 (dtd with transition to higher order splitting, $J_{4,3\text{-}H(A)}$ = 9.8 Hz, $J_{4,5}$ = 6.1 Hz, $J_{4,3\text{-}H(B)}$ = 2.5 Hz, 4-H), 4.04 (dddd, $J_{2,3\text{-}H(A)}$ = 10.4 Hz, $J_{2,1\text{-}H(A)}$ = 6.6 Hz, $J_{2,1\text{-}H(B)}$ = 3.8 Hz, $J_{2,3\text{-}H(B)}$ = 3.1 Hz, 2-H), 4.48 (s, 1′-H_2), 5.09–5.14 (m, 7-H_E, 7-H_Z), 5.82 (m_c, 6-H), AA′BB′ signal centered at δ = 6.88 and δ = 7.25 (C_6H_4).
^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 38.71 and 42.21 (C-3, C-5), 55.26 (OCH_3), 71.02, 71.16, 73.05, and 73.99 (C-1, C-2, C-4, C-1′), 113.86 and 129.41 (2 × C_{ortho}, 2 × C_{meta}), 117.86, 129.89, 134.51, and 159.35 (C-6, C-7, C_{para}, C_{ipso}).
IR(film): 3400, 3075, 2915, 2860, 1640, 1615, 1585, 1515, 1460, 1440, 1365, 1300, 1250, 1175, 1100, 1035, 990, 920, 820 cm^{-1}.
Anal. Calcd for $C_{15}H_{22}O_4$ (266.3): C, 67.64; H, 8.33. Found: C, 67.54; H, 8.39.
(25) (a) Rychnovsky, S. D.; Skalitzky, D. J. *Tetrahedron Lett.* **1990**, *31*, 945. (b) Rychnovsky, S. D.; Rogers, B.; Yang, G. *J. Org. Chem.* **1993**, *58*, 3511. (c) Evans, D. A.; Rieger, D. L.; Gage, J. R. *Tetrahedron Lett.* **1990**, *31*, 7099.
(26) The asymmetric desymmetrization of a bicyclic, tertiary dialkenylcarbinol by the zirconium analog of a SAE, employing 3.0–3.4 equivalents each of Zr(*i*-PrO)$_4$, D-(–)-diisopropyl tartrate, and *t*-BuOOH is described in: Spivey, A. C.; Woodhead, S. J.; Weston, M.; Andrews, B. I. *Angew. Chem. Int. Ed.* **2001**, *40*, 769; *Angew. Chem.* **2001**, *113*, 791.