C-1 Reactivity of 2,3-Epoxy Alcohols via Oxirane Opening with Metal Halides: Applications and Synthesis of Naturally Occurring 2,3-Octanediol, Muricatacin, 3-Octanol, and 4-Dodecanolide

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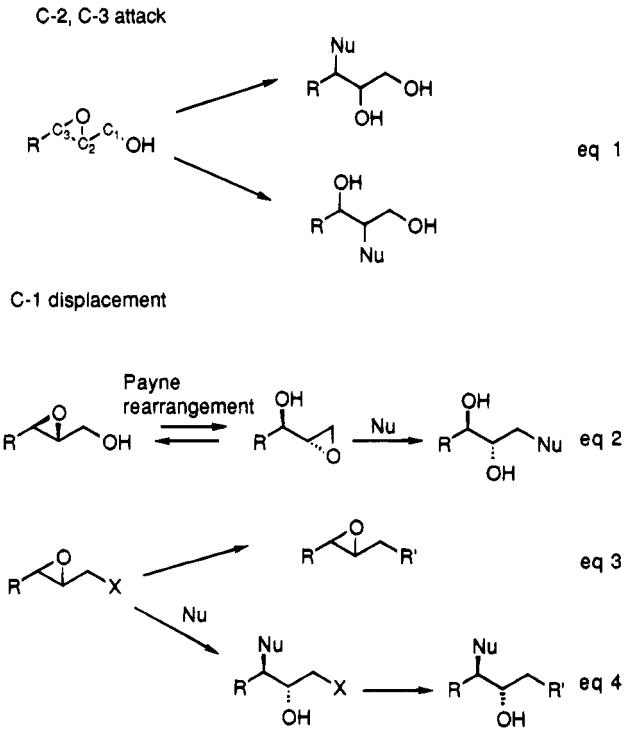
The C-1 reactivity of 2,3-epoxy alcohols and derivatives has been examined thoroughly. In the first approach a rearrangement opening of 2,3-epoxy alcohols with LiI leads to 1-iodo 2,3-diols with *erythro* or *threo* stereochemistry starting from *trans* or *cis* epoxy alcohols. Subsequent coupling with a carbon nucleophile can lead to a series of vicinal diols with predicted relative and absolute stereochemistry: the described methodology has been applied to the asymmetric synthesis of the naturally occurring (*S*,*S*)-2,3-octanediol and (*R*,*R*)-muricatacin. The second approach, starting from easily available tosyloxy epoxides, leads to the highly regioselective opening of the oxirane ring with Li halides. The 3-iodohydrins obtained can be reduced to the corresponding 1-(tosyloxy)-alkan-2-ols and then coupled with common carbon nucleophiles to afford, in high yields, optically active alcohols. This methodology has been applied to the asymmetric synthesis of naturally occurring pheromones like 3(*R*)-octanol and 4(*R*)-dodecanolide.

2,3-Epoxy alcohols, obtained in enantiomerically enriched form by the standard asymmetric epoxidation (AE),[1] continue to be attractive starting materials for the synthesis of natural products. In fact, a subsequent regioselective opening of the oxirane ring can provide a large variety of chiral synthons with different functionalities.[2] In principle there are three reactive sites in the 2,3-epoxy alcohols: two are related to the nucleophilic opening of the epoxy ring (C-2 and C-3), leading to the formation of 1,2- or 1,3-diols with various substituents (see Scheme 1, eq 1). To this end the epoxy ring has been successfully opened in regio-, chemo-, and stereocontrolled fashion by a large variety of carbon nucleophiles[3] as well as by oxygen,[2a] sulfur,[2a] nitrogen,[4] and halogens.[5]

The potential reactivity of the C-1 position has been less explored, since the hydroxyl group often needs to be transformed to exploit its latent reactivity: nevertheless, the formation of a new carbon–carbon bond in this position is highly valuable for possible chain elongation. The only useful synthetic application of C-1 nucleophilic substitution of unactivated 2,3-epoxy alcohol was reported by Sharpless as a "Payne rearrangement opening reaction"[6] (see Scheme 1, eq 2). Here the nucleophile (mainly PhS^-), in the presence of the equilibrating mixture of the epoxy alcohol in the alkaline medium, reacts with the 1,2-epoxy-3-ol: the reaction is then moved

Scheme 1



to the final C-1-substituted 2,3-diol with C-2 inversion and final *erythro* stereochemistry of the two hydroxyl groups starting from the *trans* epoxy alcohol. Although employed in some applications[7] this methodology often suffers incomplete reaction (due to the equilibrium of the reactions in favor of the starting 2,3-epoxy alcohol) and competitive C-2 opening and appears better suitable to obtain *threo* diols.[8]

On the contrary, direct formation of a new carbon–carbon bond at C-1, *via* activation of the hydroxyl group

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(1) (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. (b) Johnson, R. A.; Sharpless, K. B. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.: Pergamon Press: Oxford, 1991; Vol. 7, Chapter 3.2.

(2) For general reviews see: (a) Rossiter, B. E. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; Vol. 5, Chapter 7. (b) Hanson, R. M.; *Chem. Rev.* **1991**, *91*, 437.

(3) For recent examples see: (a) Rama Rao, A. V.; Chakraborty, T. K.; Purandare, A. V. *Tetrahedron Lett.* **1990**, *31*, 1443. (b) Skrydstrup, T.; Bènèchie, M.; Kuong-Huu, F. *Tetrahedron Lett.* **1990**, *31*, 7145 and references therein.

(4) Mitsunobu, O. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.: Pergamon Press: Oxford, 1991; Vol. 6, pp 4–9.

(5) See review: Bonini, C.; Righi, G. *Synthesis* **1994**, 225.

(6) Behrens, C. H.; Ko, S. Y.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 5687.

(7) Ko, S. Y.; Lee, A. W. M.; Masamune, S.; Reed, L. A., III; Sharpless, K. B.; Walker, F. J. *Tetrahedron* **1990**, *46*, 245 and references therein.

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without the concomitant opening of the epoxy ring (Scheme 1, eq 3), appears to be a feasible way only if subsequent regioselective opening of the epoxide is not required.[9] A more feasible way would be the preliminary opening of the epoxy ring by a nucleophile (eventually easily removable), followed by the C-1 reaction (Scheme 1, eq 4).

We have recently reported some preliminary studies on two different approaches to this purpose, and in the following a more complete study and some synthetic applications of our procedures will be extensively outlined.

Results and Discussion

Rearrangement of 2,3-Epoxy Alcohols to 1-Iodo 2,3-Diols and Subsequent Transformation. We have recently shown[10] that 1-iodo 2,3-diols can be obtained from the corresponding 2,3-epoxy alcohols by the use of LiI in DME at 70 °C (see Scheme 2): this unusual rearrangement occurs with complete chemo-, regio-, and stereoselective fashion and with good chemical yields. Starting from the *trans*-2,3-epoxy alcohols the corresponding 1-iodo 2,3-*threo*-diols are obtained (eq 5), while from the *cis* epoxy alcohols the 1-iodo 2,3-*erythro*-diols can be obtained (eq 6). These stereochemical results have suggested a possible mechanism for the ring-opening rearrangement which has been clearly demonstrated.[10] Some particular reaction conditions are required, and the complete typical procedure is reported below in the Experimental Section.[11]

Scheme 2

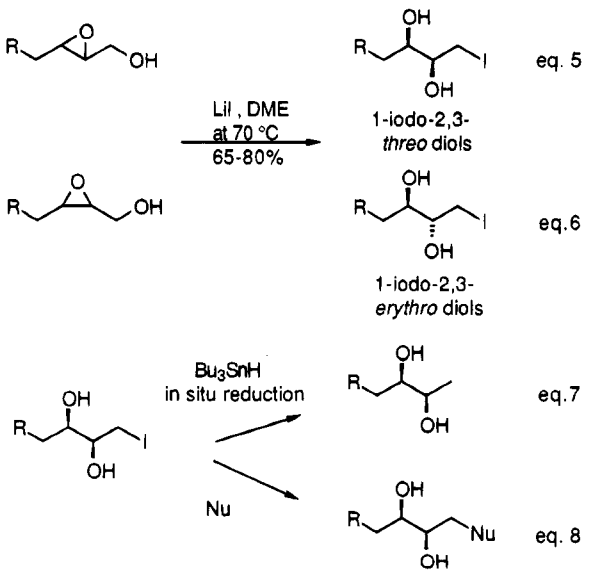
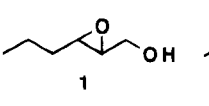
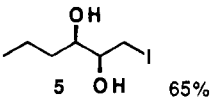
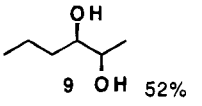
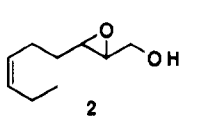
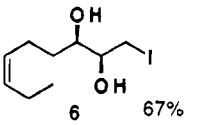
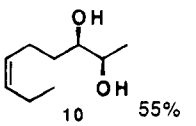
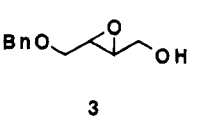
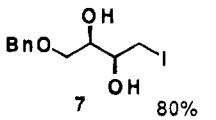
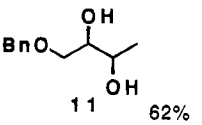
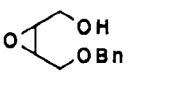
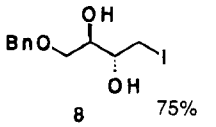
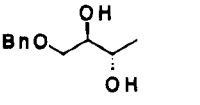


Table 1. Rearrangement Opening of 2,3-Epoxy Alcohols with LiI to 1-Iodo 2,3-Diols and "in Situ" Reduction

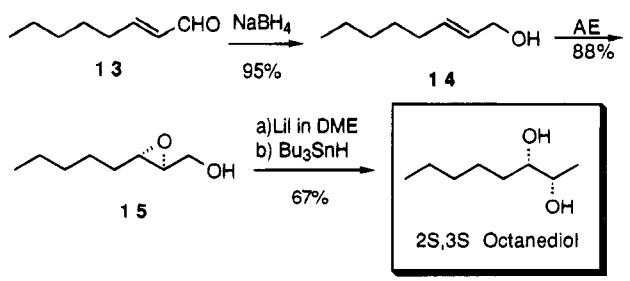
2,3-epoxy alcohols	1-iodo 2,3-diols, % yield	2,3-diols, % yield[a]
 1	 5 65%	 9 52%
 2	 6 67%	 10 55%
 3	 7 80%	 11 62%
 4	 8 75%	 12 61%

[a] Overall yield from starting 2,3-epoxy alcohol.

The iodohydrins obtained can be utilized for further synthetic transformations (Scheme 2, eqs 7 and 8). Reduction, via free radicals, can lead to 2,3-diols of known relative configuration as shown in eq 7. As already shown in other related oxirane opening of epoxides with metal halides,[12] the halogenation–reduction sequence can be performed, in most of the cases, in one step without the isolation of the intermediate iodohydrin. Table 1 shows some representative examples of the rearrangement opening and subsequent reduction of both *trans* and *cis* epoxy alcohols (compounds **1**–**4**) leading, respectively, to *erythro* and *threo* diols.

The described overall procedure has been applied to a straightforward synthesis of the pheromone (2*S*,3*S*)-octanediol[13] (see Scheme 3). Starting with commercially available aldehyde **13**, the alcohol **14**[14] was subjected to AE, affording the chiral epoxy alcohol **15** (ee > 98%). Finally **15** was treated with LiI and then reduced "in situ" to the final (2*S*, 3*S*)-octanediol in a three-step sequence

Scheme 3. Synthesis of (2*S*,3*S*)-Octanediol



(8) A major limitation in this strategy appears when a final *threo* diol is desired; in fact a lower ee normally is obtained in the AE of the (*Z*) allylic alcohols. The more recent Sharpless asymmetric dihydroxylation (AD) offers major advantages over the AE strategy, mainly (a) if a final *threo* diol is desired and (b) if the starting (*E*) olefin is easily available and is a good substrate for the AD. (For AD see: Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993, pp 227–272 and references therein.)

(9) Direct tosyl replacement of 1-(tosyloxy)-2,3-epoxides was reported by: Mori, K.; Ebata, T. *Tetrahedron Lett.* **1981**, *22*, 4281. 1-Halo-2,3-epoxides, obtained from the corresponding epoxy alcohols via tosyl derivatives, have also been coupled with vinyl Grignard reagents, see: Nicolau, K. C.; Guggan, M. E.; Ladduwahetty, T. *Tetrahedron Lett.* **1984**, *25*, 2069.

(10) Bonini, C.; Giuliano, C.; Righi, G.; Rossi, L. *Tetrahedron Lett.* **1992**, *33*, 7429.

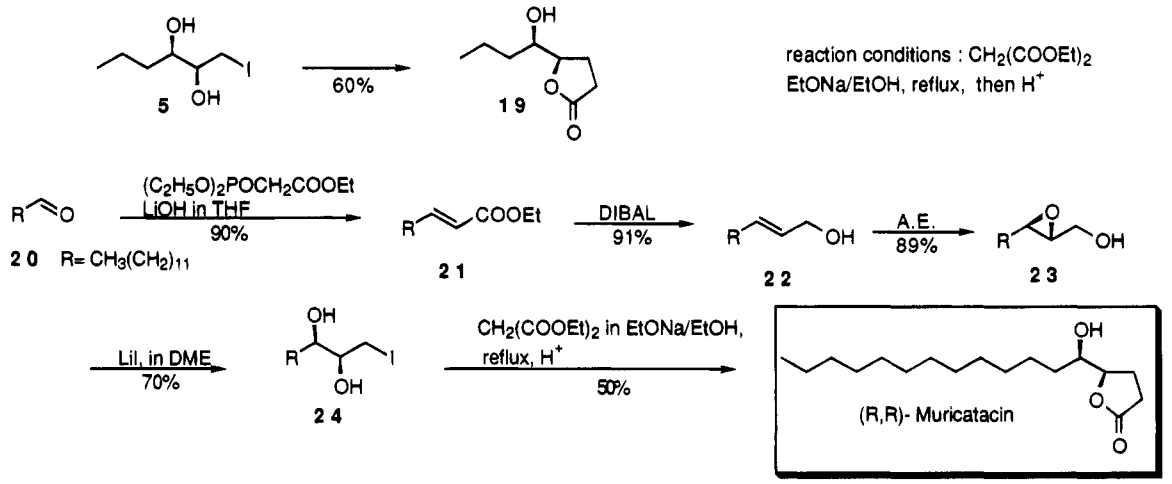
(11) The reaction results were particularly sensitive to the halogen and to the cation species. In fact, when LiBr was used, only 40% yield of the corresponding bromohydrin could be obtained, while the use of LiCl did not give any reaction. On the other hand, the use of other metal iodides such as NaI, KI, and CuI_2 did not give any appreciable reaction after several hours.

(12) (a) Bonini, C.; Di Fabio, R. *Tetrahedron Lett.* **1988**, *29*, 819. (b) Bonini, C.; Di Fabio, R.; Sotgiu, G.; Cavagnero, S. *Tetrahedron* **1989**, *45*, 2896. (c) Bonini, C.; Righi, G.; Sotgiu, G. *J. Org. Chem.* **1991**, *56*, 6206. (d) Bonini, C.; Righi, G. *Tetrahedron* **1992**, *48*, 1531.

(13) Ibwabuchi, K. *Appl. Entomol. Zool.* **1982**, *17*, 494.

(14) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.

Scheme 4. Coupling of 1-Iodo 2,3-Diol with Malonate to the Preparation of 5-Hydroxy γ-Lactones: Synthesis of (*R,R*)-Muricatacin

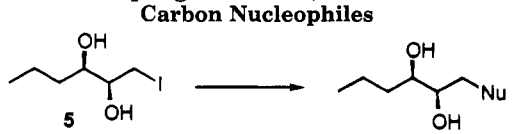


which represents, so far, the shortest preparation of the title compound.[15]

As an additional application, the potential replacement of the iodine by carbon nucleophilic reagents would be highly valuable to the formation of a new carbon–carbon bond with the preparation of a large variety vicinal chiral diols (Scheme 2, eq 8).

As shown in Table 2 the representative 1-iodo 2,3-diol **5** has been subjected to coupling with some organocuprates, leading to the corresponding aliphatic (compound **16**), aromatic (compound **17**), or homoallylic (compound **18**) *threo* diols. The overall yields of these reactions are quite high, and the 1-iodo 2,3-diols can be directly subjected to the coupling reaction without the need for hydroxyl protection. Also the direct coupling of compound **5** with the malonate (see Scheme 4) afforded the corresponding 5-hydroxy-γ-lactone **19** in reasonable yield (see Experimental Section), showing a new entry to this important class of chiral hydroxy lactone.

Table 2. Coupling of 1-Iodo-2,3-hexanediol 5 with Carbon Nucleophiles

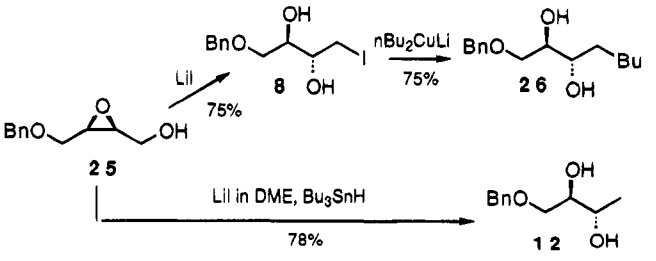


entry	nucleophile	% yield	product
1	nBu_2CuLi	90	**16**
2	Ph_2CuLi	95	**17**
3	$(CH_3CH{=}CH)_2CuLi$	92	**18**

This procedure for the preparation of 5-hydroxy-γ-lactones has been applied to the asymmetric synthesis of (*R,R*)-muricatacin, a recently isolated (from the seeds of *Annona muricata*) acetogenin derivative with some cytotoxic activity on human tumor cell lines.[16] The reaction sequence starts from commercially available aldehyde **20** (Scheme 4) by standard homologation to the allylic alcohol **22**; the subsequent AE was then followed by the rearrangement of the chiral 2,3-epoxy alcohol **23** (ee > 97%) with LiI. The final coupling of the iodohydrin **24** with malonate afforded natural muricatacin in a five-step sequence with reasonable yield.[17]

The described procedure, when starting from (*Z*) allylic alcohols, would lead to the corresponding *erythro* diols (see Scheme 2, eq 6): this sequence can offer an alternative to the known procedure to obtain *erythro* diols starting from the corresponding (*E*) allylic alcohols followed by AE and Payne rearrangement (see Scheme 1, eq 2).[6] More recently (*E*) allylic alcohols have been subjected to the Sharpless asymmetric dihydroxylation (AD) followed by a cyclic sulfate rearrangement opening, leading to *erythro* diols.[18] For comparison with this last methodology we have prepared chiral *erythro* diols by our procedure. The known chiral 1-benzyl-2-epoxybutan-4-ol **25**[14] (prepared in two steps from the commercially available (*Z*)-1-(benzyloxy)-2-buten-4-ol) was transformed (see Scheme 5) into the *erythro* diol **26** via LiI epoxide rearrangement and subsequent coupling with lithium dibutylcuprate. Alternatively the in situ radical reduction of the iodohydrin afforded directly compound **12**. The overall three-step sequence (from the (*Z*) allylic alcohol) proceeds with a 60% overall yield for compound **26** and a 67.5% overall yield for compound **12**, which compare favorably with the four-step sequence employing the cyclic sulfate rearrangement procedure to prepare **26** and **12**.[18]

Scheme 5. Synthesis of Optically Active *Erythro* Diols



Ring Opening of 1-(Tosyloxy)-2,3-epoxides to 3-Halo-1-(tosyloxy)-2-alkanols and Subsequent C-1

(15) For recent syntheses of (2*S*,3*S*)-octanediol see: (a)Mori, K.; Otsuka, T. *Tetrahedron* **1985**, *41*, 553. (b) Bel-Rhlid, R.; Fauve, A.; Vrschambre, H. *J. Org. Chem.* **1989**, *54*, 3221, and ref 12d.

(16) Rieser, M. J.; Kozlowski, J. F.; Wood, K. V.; McLaughin, J. L. *Tetrahedron Lett.* **1991**, *32*, 1137.

(17) For recent syntheses of muricatacin see: (a) Wang, Z. M.; Zhang, X. L.; Sharpless, K. B.; Sinha, S. C.; Sinha-Bagchi, A.; Keiman, E. *Tetrahedron Lett.* **1992**, *33*, 6407. (b) Gravier-Pelletier, C.; Sanierè, M.; Charvet, I.; Le Merrer, Y.; Depezay, J. C. *Tetrahedron Lett.* **1994**, *35*, 115. (c) Marshall, J. A.; Welmaker, G. S. *J. Org. Chem.* **1994**, *59*, 4122 and references therein.

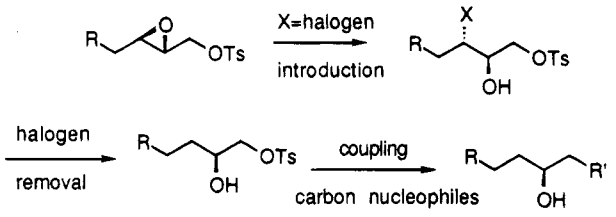
(18) Ko, S. Y.; Malik, M.; Dickinson, A. F. *J. Org. Chem.* **1994**, *59*, 2570.

Elaboration. The 1-(tosyloxy) 2,3-epoxides appear to be particularly attractive compounds, since they can be prepared in optically active form by in situ derivatization of the corresponding 2,3-epoxy alcohols prepared by AE.[14]

The potential reactivity of the C-1 carbon of the epoxy alcohols, with the direct displacement of a preformed leaving group (see Scheme 1, eq 3), has been utilized only in a few cases with carbon[9] or heteroatom nucleophiles[19] because of competitive ring opening.

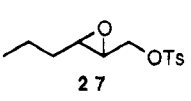
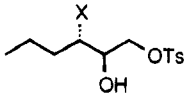
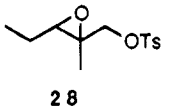
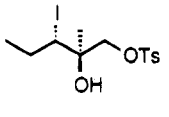
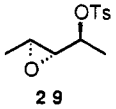
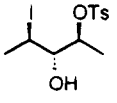
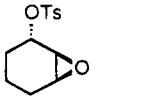
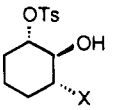
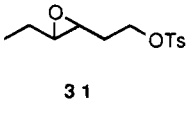
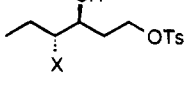
We have chosen the alternative route outlined in Scheme 6, in which a 1-(tosyloxy) 2,3-epoxide, if regioselectively opened by, i.e., halogens, can be transformed into the corresponding 3-halohydrin: this halohydrin can be conveniently reduced and then coupled with common carbon nucleophiles, leading to an unlimited series of chiral alcohols.

Scheme 6



A preliminary study on the regioselective preparation of 1-(tosyloxy)-3-halo-2-alkanols and other related tosyloxy epoxides was recently performed by us;[20] we utilized two of our developed methodologies which have already been used on simple epoxides and epoxy alcohols.[12c,21] The results with the use of Li halides[21] (see Table 3 for representative examples) are particularly positive both in regio and chemical yields; also noteworthy are the excellent results obtained with secondary tosylates like **29**, cyclic epoxy tosylates like compound **30**, and also homoallylic epoxy alcohols like compound **31**.[22]

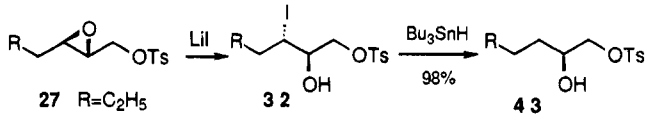
Table 3. Regioselective Opening of Tosyloxy Epoxy Alkane with LiX in CH_3CN, Amberlyst 15

tosyloxy epoxide	main halohydrin	% yield
 **27**		**32** X=I 99% **33** Br 99% **34** Cl 99%
 **28**		**35** 99%
 **29**		**36** 99%
 **30**		**37** X= I 99% **38** Br 99% **39** Cl 92%
 **31**		**40** X= I 90% **41** Br 55% **42** Cl 90%

This reaction procedure, with the use of LiX in CH_3CN and Amberlyst 15, appears unprecedented for the mildness of the reaction conditions (room temperature, use of commercial solvents without purification or work up). Furthermore it allows the preparation of I, Br, and Cl halohydrins and therefore compared favorably with the other known procedure.[23] These halohydrins are themselves also attractive starting materials for the synthesis of natural halogen-containing marine products.[24]

If the final 1-(tosyloxy)-2-alkanol is desired, the halohydrins can be conveniently reduced with Bu_3SnH and AIBN with high yield (see Scheme 7, from compound **27** to the final diol **43**).

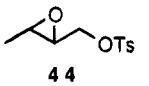
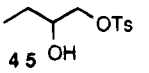
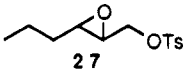
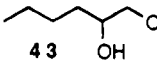
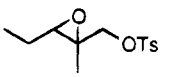
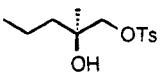
Scheme 7



27 R=C_2H_5 **32** **43**

With MgI_2 (already used in opening epoxy alcohols and derivatives[12c]) the results appear less reliable: the methodology appears suitable only in some cases, if the final 1-(tosyloxy) alkanol is desired, since the reduction of the iodohydrin can be performed in situ (see Table 4 for representative examples for the opening–reduction one-pot sequence). However, in most of the cases, we recommend performing the opening of the oxirane ring with the LiI/Amberlyst 15 procedure, followed by reduction via free radicals, since both reactions are extremely high yielding and easily conducted.

Table 4. Regioselective Opening and "in Situ" Reduction of 1-(Tosyloxy)-2,3-epoxyalkanes with MgI_2 and Bu_3SnH to 1-(Tosyloxy)alkan-2-ols

1-(tosyloxy)-2,3-epoxyalkane	1-(tosyloxy)-alkan-2-ol	% yield
 **44**	 **45**	83%
 **27**	 **43**	67%
 **28**	 **46**	40%

It is noteworthy that, in both reaction procedures used, no trace of corresponding tosyl displacement by iodine has been observed: however, this can be conveniently performed, if desired, as reported below.

During the preparation of our manuscript a paper appeared that described the direct reduction of 1-(tosyl-

(19) (a) Klunder, J. M.; Ko, S. Y.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 3710.

(20) Federici, C.; Righi, G.; Rossi, L.; Bonini, C.; Chiummientu, L.; Funicello, M. *Tetrahedron Lett.* **1994**, *35*, 797.

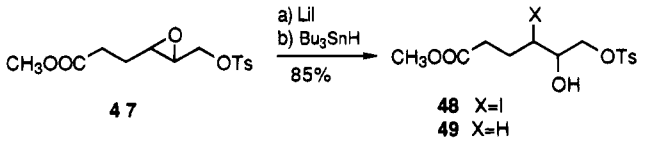
(21) Bonini, C.; Giuliano, C.; Righi, G.; Rossi, L. *Synth. Commun.* **1992**, *22*, 1863.

(22) The procedure has been applied to other epoxy tosylates not reported (C_4 and C_8 1-(tosyloxy) 2,3-epoxides) always with excellent regio and chemical yields. Only in the case of C-3-substituted 1-(tosyloxy) 2,3-epoxides did the reaction proceed with much longer reaction time and somewhat lower regioselectivity, with the formation of several side products.

(23) Gao, L.; Saitoh, H.; Feng, F.; Murai, A. *Chem. Lett.* **1991**, 1787. The procedure described herein afforded in excellent regio and chemical yields the corresponding halohydrins: however, the reaction is limited to chloro- and bromohydrins and must be performed at lower temperatures (−15 to −55 °C).

oxy)-2-epoxides to the corresponding 1-(tosyloxy)-2-alkanols, by the use of DIBAL.[25] Although the latter appears to be a simpler procedure, we believe that our method is more general: i.e., as shown in Scheme 8, a compound like **47**[26] was conveniently opened and then reduced, chemoselectively, to the final compound **49**, whereas the use of a reducing agent like DIBAL would also have reduced the carboxyl function. Furthermore, the use of DIBAL has not been yet tested on other different compounds like **29**, **30**, or **31** (see Table 3).

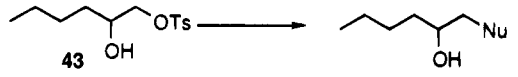
Scheme 8



47 **48** X=I **49** X=H

The final 1-(tosyloxy)-2-alkanols can be subjected to classical coupling reactions with common carbon nucleophiles, as shown with the representative compound **43** (see Table 5). The reaction proceeds with good to excellent yield, also with vinylcuprates: in the latter case (compound **52**) homoallylic alcohols, which are well-known substrates for the obtaining via iodocyclization reaction[27] of *syn* 1,3-diols, are obtained.

Table 5. Coupling of 1-(Tosyloxy)hexan-2-ol (43) with Carbon Nucleophiles

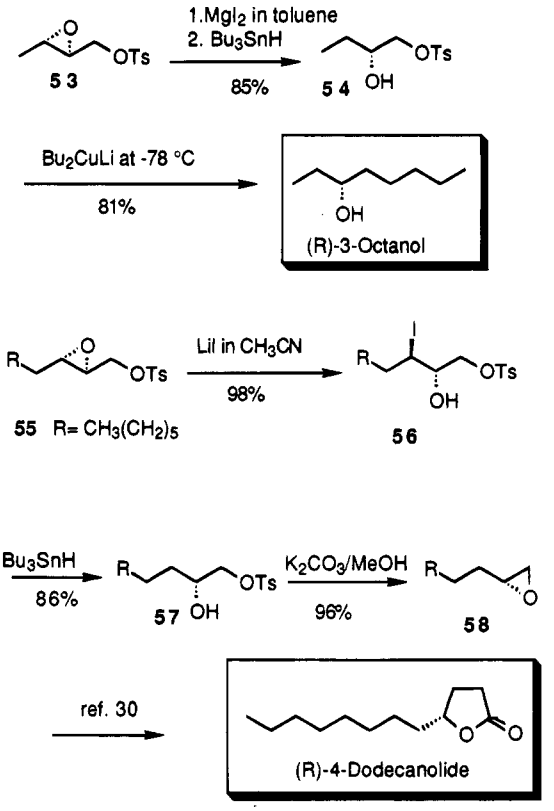


43

entry	nucleophile	% yield	product
1	nBu_2CuLi	78	**50**
2	Ph_2CuLi	87	**51**
3	$(CH_3CH{=}CH)_2CuLi$	85	**52**

The described procedure has been applied to the synthesis of two naturally occurring pheromones (see Scheme 9). Starting from known optically active epoxytosylate **53**,[14] the "one-pot" procedure afforded in high yield the alcohol **54**: this was then coupled with lithium dibutylcuprate affording in a short, high-yielding sequence the pheromone 3(*R*)-octanol.[28] Similarly, optically active compound **55** (prepared from the corresponding chiral epoxy alcohol[14]) was opened with LiI to the iodohydrin **56** and then reduced to the diol **57**; since the direct coupling with malonate did not always give satisfactory results,[29] **57** was transformed to the known epoxide **58**, which has already been converted[30] to the final pheromone 4(*R*)-dodecanolide.[31]

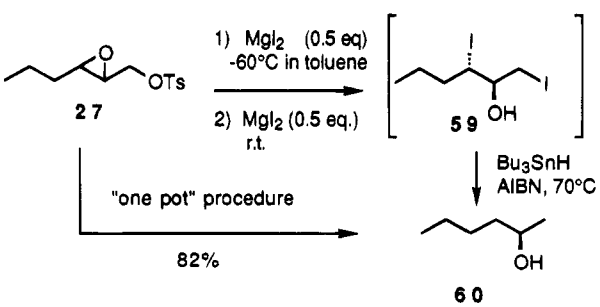
Scheme 9. Synthesis of Optically Active Pheromones



53 **54** **55** **56** **57** **58**

As already noted, tosyl replacement by iodine or other halogens was not observed. However, this can be performed with the use of MgI_2 (not with the LiX/Amberlyst procedure). In fact, after the ring opening (see Scheme 10 for representative compound **27**), the tosyl replacement can be subsequently performed with the use of another equivalent of MgI_2 at room temperature. The eventually isolated diiodohydrin **59** (see Experimental Section) leads by reduction with Bu_3SnH to the final 2-alkanol **60**. The overall one-pot sequence represents an efficient route to enantiomerically pure 2-alkanols starting from chiral epoxy alcohols. The sequence has high advantages, in terms of chemoselectivity, with respect to other procedures involving reduction of 1-(tosyloxy)-2,3-epoxides to the corresponding 2-alkanols with common hydride reagents[32] and makes this methodology available for the preparation of many natural products possessing this structural feature.[33]

Scheme 10. Chemoselective Preparation of 2-Alkanols



27 **59** **60**

In conclusion the reaction of chiral 2,3-epoxy alcohols or tosylates with Li halides or MgI_2 was shown to be easily performed: the obtaining, in a regio-, chemo-, and

(24) For reviews see: Moore, R. E. In *Marine Natural Products*; Scheuer, P. J., Ed.; Academic Press: New York, 1978; Vol. 1, Chapter 2. Fenical, W. In *Marine Natural Products*; Scheuer, P. J., Ed.; Academic Press: New York, 1980; Vol. 2, p 174. Barrow, K. D. In *Marine Natural Products*; Scheuer, P. J., Ed.; Academic Press: New York, 1983; Vol. 5, p 51. Erickson, K. L. In *Marine Natural Products*; Scheuer, P. J., Ed.; Academic Press: New York, 1983; Vol. 5, p 131. Faulkner, D. J. *Nat. Prod. Rep.* **1984**, 251; **1986**, 1.

(25) Chong, J. M.; Johannsen, J. *Tetrahedron Lett.* **1994**, *35*, 7197.

(26) Compound **47** was prepared from known epoxy alcohol **2** in the following sequence (see also Experimental Section): (a) tosylation (TsCl in CH_2Cl_2, Et_3N, DMAP); (b) ozonolysis; (c) oxidation ($RuCl_3$); (d) esterification (CH_2N_2).

(27) (a) Cardillo, G.; Orenoe, M.; Porzi, G.; Sanzi, S. *J. Chem. Soc., Chem. Commun.* **1981**, 465. (b) Lipshutz, B. H.; Kozlowski, J. A. *J. Org. Chem.* **1984**, *49*, 1149.

(28) For several approaches to the synthesis of (*R*)-3-octanol see: Mori, K. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; John Wiley & Sons Inc.: New York, 1992; Vol. 9, pp 108–109.

stereoselective fashion, of differently functionalized halohydrins can be utilized in the straightforward preparation of a large variety of substituted chiral diols or alkanols, as also demonstrated with the reported synthesis of some natural products. We believe this can further expand the synthetic utility of the AE and the subsequent manipulation of the chiral 2,3-epoxy alcohols.

Experimental Section

General. ^{1}H and ^{13}C-NMR spectra were recorded at 200 and 50.3 Hz, respectively. Epoxy alcohols were prepared from the corresponding allylic alcohols following the standard procedure, and references are given for known compounds. 1-(Tosyloxy)-2,3-epoxy alcohols were prepared following the in situ procedure,[14] and a representative procedure is given for compound **27**. Secondary tosyloxy−epoxides were prepared from the corresponding epoxy alcohols, and a representative procedure is given for compound **29**. AE were performed on the corresponding allylic alcohols following the literature procedure, and a representative procedure is given for compound **15**. The enantiomeric excess of the chiral epoxy alcohols was measured by ^{1}H-NMR analysis with Eu(hfc)$_3$ or via Mosher derivatives prepared by standard procedures. Reactions were monitored by TLC using Merck silica gel 60 F-254 plates with UV indicator (tosylates and iodohydrins) and/or visualized with phosphomolybdic acid (10% solution in EtOH). Flash column chromatography on silica gel was normally used for purification of the reaction mixtures. Regioisomeric ratios for compounds **32**−**42**, **45**, and **46** were determined by analysis of the ^{1}H-NMR spectra of the reaction mixtures before purification. All solvents, unless specified, were purified before use with standard drying procedures.

General Procedure for the Reaction of 2,3-Epoxyalkan-1-ols with LiI to the Corresponding 1-Iodo 2,3-Diols and then in Situ Reduction to 2,3-Diols: Representative Procedure for the Preparation of (2*R,3*R**)-1-Iodo-2,3-hexanediol (5) and (2*R**,3*R**)-2,3-Hexanediol (9).** To a solution of 2,3-epoxyhexan-1-ol **1**[12c] (116 mg, 1 mmol) in DME (10 mL) in a round bottom flask equipped with a condenser and magnetic stirrer, LiI (4 mmol) was added. The reaction mixture was warmed at 70 °C, and after 7 h (TLC monitoring with UV lamp) the reaction was stopped. After addition of EtOAc (50 mL) the organic layer was washed with saturated $Na_2S_2O_3$. The organic layer was then dried over Na_2SO_4 and then evaporated in vacuo. The crude mixture was then chromatographed on silica gel (hexane/ether 8:2), affording pure **5** (159 mg, 65%). ^{1}H-NMR ($CDCl_3$) δ 3.74−3.60 (1H, m), 3.56−3.42 (1H, m), 3.42−3.20 (2H, m), 1.62 (2H, bs), 1.60−1.22 (4H, m), 0.92 (3H, t, J = 7.4 Hz). ^{13}C-NMR ($CDCl_3$) δ 73.5, 72.7, 35.7, 18.5, 13.8, 10.3.

To obtain directly the 2,3-diol **9**, after the reaction of **1** with LiI (TLC monitoring), AIBN (catalytic, 10 mg) and Bu_3SnH (350 mg, 1.2 mmol) were added at 80 °C: after 1 h (TLC monitoring) the reaction was stopped and most of the solvents were removed in vacuo. The concentrate was diluted with CH_3CN (50 mL) and washed with hexane (5 mL, three times) to remove most of the tin residues. The solvent was evaporated in vacuo, affording a crude mixture which was then chromatographed on silica gel (hexanes/ether 9:1) to give pure compound **9** as colorless oil (61 mg, 52% from **1**). ^{1}H-NMR ($CDCl_3$) δ 3.62−3.45 (1H, m), 3.36−3.24 (1H, m), 2.55 (2H, bs,), 1.62−1.20 (4H, m), 1.15 (3H, d, J = 6.1 Hz), 0.91 (3H, t, J = 6.9 Hz). ^{13}C-NMR ($CDCl_3$) δ 75.8, 70.7, 35.2, 19.2, 18.5, 13.8. Anal. Calcd for $C_6H_{14}O_2$: C, 60.97; H, 11.95. Found: C,61.06; H, 11.84.

(2*R,3*R**,6*Z*)-1-Iodo-6-nonen-2,3-diol (6).** According to the general procedure, compound **2**[12c] (144 mg) gave pure compound **6** (175 mg, 67%). ^{1}H-NMR ($CDCl_3$) δ 5.60−5.23 (2H, m), 3.70−3.60 (1H, m), 3.55−3.42 (1H, m), 3.40−3.20 (2H, m), 2.60 (2H, bs), 2.30−1.90 (4H, m), 1.62−1.48 (2H, m), 0.95 (3H, t, J = 8.9 Hz). ^{13}C-NMR ($CDCl_3$) δ 133.0, 128.0, 73.7, 72.7, 33.6, 23.0, 20.4, 14.1, 10.2.

(2*R,3*R**)-1-Iodo-4-(benzyloxy)-2,3-butanediol (7).** According to the general procedure, compound **3**[10] (72 mg) gave pure compound **7** (97 mg, 80%). ^{1}H-NMR ($CDCl_3$) δ 7.32 (5H, bs), 4.52 (2H, s), 3.96−3.85 (1H, m), 3.72−3.65 (1H, m), 3.60−3.52 (2H, m), 3.36−3.20 (2H, m), 3.08 (2H, bs). ^{13}C-NMR ($CDCl_3$) δ 137.5, 128.6, 128.1, 127.9, 73.5, 71.9, 70.9, 8.3.

(2*R,3*S**)-1-Iodo-4-(benzyloxy)-2,3-butanediol (8).** According to the general procedure, compound **4**[14] (88 mg) gave pure compound **8** (109 mg, 75%). ^{1}H-NMR ($CDCl_3$) δ 7.32 (5H, bs), 4.55 (2H, s), 3.75−3.62 (3H, m), 3.58−3.35 (3H, m), 2.58 (2H, bs). ^{13}C-NMR ($CDCl_3$) δ 137.6, 128.7, 128.6, 128.2, 127.9, 73.6, 72.1, 71.8, 70.9, 12.4.

(2*R,3*R**,6*Z*)-6-Nonen-2,3-diol (10).** According to the general one-pot procedure, compound **2** gave pure compound **10** (45 mg, 55%). ^{1}H-NMR ($CDCl_3$) δ 5.58−5.24 (2H, m), 3.68−3.48 (1H, m), 3.41−3.27 (1H, m), 2.36−1.88 (6H, m), 1.59−1.35 (2H, m), 1.17 (3H, d, J = 6.3 Hz), 0.94 (3H, t, J = 7.5 Hz). ^{13}C-NMR ($CDCl_3$) δ 132.7, 128.4, 75.7, 70.7, 33.1, 23.1, 20.3, 19.2, 14.1. Anal. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.47. Found: C, 68.35; H, 11.42.

(2*R,3*R**)-1-(Benzyloxy)-2,3-butanediol (11).** According to the general procedure, compound **3** (85 mg) gave pure compound **11** (54 mg, 62%). ^{1}H-NMR ($CDCl_3$) δ 7.32 (5H, bs), 4.52 (2H, s), 3.90−3.40 (4H, m), 2.74 (1H, d, J = 5.3 Hz), 2.64 (1H, d, J = 4.9), 1.18 (3H, d, J = 5.3 Hz). ^{13}C-NMR ($CDCl_3$) δ 137.8, 128.6, 128.1, 127.9, 73.9, 73.6, 72.3, 68.3, 19.0. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.38; H, 8.19.

(2*R,3*S**)-1-(Benzyloxy)-2,3-butanediol (12).** According to the general procedure compound **4** (155 mg) gave pure compound **12** (96 mg, 61%). ^{1}H-NMR ($CDCl_3$) δ 7.32 (5H, bs), 4.55 (2H, s), 3.92−3.78 (1H, m), 3.75−3.50 (3H, m), 2.98 (1H, bs), 2.63 (1H, bs), 1.13 (3H, d, J = 6.5 Hz). ^{13}C-NMR ($CDCl_3$) δ 137.8, 128.6, 128.0, 127.9, 73.5, 73.2, 70.9, 68.7, 18.0. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.35; H, 8.20.

(2*E*)-2-Octen-1-ol (14). A three-necked round bottom flask, with a nitrogen inlet and a stirring apparatus was charged, at 0 °C, with commercially available *trans*-2-octenal **13** (1.5 g, 11.9 mmol) dissolved in MeOH (4 mL). To the solution was then slowly added $NaBH_4$ (0.226 g, 5.9 mmol) dissolved in MeOH (7 mL). After 3 h the reaction was quenched with brine (10 mL) and extracted with Et_2O (50 mL). The organic layer was then extracted with brine until neutral, dried over Na_2SO_4, and concentrated in vacuo, affording pure compound **14** (1.435 g, 95%), which was used for the next reaction without purification. ^{1}H-NMR ($CDCl_3$) δ 5.72−5.45 (2H, m), 4.00 (2H, d, J = 4.7 Hz), 2.40 (1H, bs), 2.02−1.90 (2H, m), 1.46−1.10 (6H, m), 0.82 (3H, t, J = 7.0 Hz). ^{13}C-NMR ($CDCl_3$) δ 133.3, 129.0, 63.4, 32.0, 31.1, 28.6, 22.2, 13.7. Anal. Calcd for $C_8H_{16}O$: C, 74.94; H, 12.58. Found: C, 74.99; H, 12.53.

(2*S*,3*S*)-2,3-Epoxyoctan-1-ol (15). To a 100 mL two-necked round bottom flask equipped with a magnetic stirrer and nitrogen inlet were added molecular sieves (3A, 300 mg) in CH_2Cl_2 (35 mL). At −20 °C and with stirring were then added L-(+)-DIPT (1.24 g, 0.6 mmol) and Ti(OiPr)$_4$ (142 mg, 0.5 mmol). After 10 min TBHP (3 M solution in octane, 6.6 mL, 20 mmol) was slowly added. The solution was stirred for 30 min, and then compound **14** (1.28 g, 10 mmol) dissolved in CH_2Cl_2 (5 mL) was added. The reaction was stopped after 3 h by addition, at 0 °C, of $FeSO_4$ (3.3 g, 12 mmol) and tartaric acid (1 g, 66 mmol) in water (10 mL). The biphasic solution was stirred for 10 min, and then, after separation, the organic layer was added with NaOH (1 mL, 30% solution in brine).

(29) The direct coupling of the tosylate with malonate appears less feasible than the corresponding coupling of the iodohydrins (see Scheme 4); probably O-alkylation becomes an important side reaction, and this does not allow reliable repetition of the direct coupling, although we have obtained good results in some cases. We suggest, therefore, transforming the 1-(tosyloxy)-2-alkanol into the corresponding epoxide, which can then be easily opened with malonate and other related carbon nucleophiles.

(30) Sugai, T.; Mori, K. *Agric. Biol. Chem.* **1984**, *48*, 2497.

(31) For several approaches to the synthesis of (*R*)-4-dodecanolide see: Mori, K. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; John Wiley & Sons Inc.: New York, 1992; Vol. 9, pp 216−220.

(32) Chong, J. M. *Tetrahedron Lett.* **1992**, *33*, 33.

(33) Many insect pheromones possess this structural feature (see ref 28, Chapter 1).

The biphasic mixture was then stirred for 1 h and diluted with water; after separation the organic layer was dried over Na_2SO_4 and concentrated in vacuo. Column chromatography (hexanes/EtOAc 7:3) afforded pure compound **15** (1.26 g, 88%). $[\alpha]_D = -42.8°$ (*c* 1.88, $CHCl_3$), ee > 98% (determined via Mosher derivative). ^{1}H-NMR ($CDCl_3$) δ 3.95–3.80 (1H, m), 3.68–3.50 (1H, m), 2.98–2.87 (2H, m), 2.00 (1H, bs), 1.62–1.12 (8H, m), 0.85 (3H, t, J = 8.4 Hz). ^{13}C-NMR ($CDCl_3$) δ 61.7, 58.4, 55.9, 31.4, 31.3, 25.4, 22.3, 13.7. Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.67; H, 11.16.

(2*S*,3*S*)-2,3-Octanediol. In a round bottom flask was added with magnetic stirring 2,3-epoxyoctan-1-ol **15** (135 mg, 0.94 mmol) dissolved in DME (10 mL). To the solution was added at 70 °C LiI (0.536 g, 4 mmol) as described in the general procedure. After 8 h (TLC monitoring with UV lamp) to the reaction mixture were added AIBN (catalytic, 10 mg) and Bu_3SnH (321 mg, 1.1 mmol). After 2 h, the solvent was evaporated in vacuo and the crude product was chromatographed (hexanes and then hexanes/ether 95:5) to afford (2*S*,3*S*)-octanediol (93 mg, 67%). $[\alpha]_D = -16.8°$ (*c* 0.9, $CHCl_3$) (lit.[15a] $[\alpha]_D = -18.5°$ ($CHCl_3$) and lit.[15b] $[\alpha]_D = -16°$ ($CHCl_3$)). ^{1}H-NMR ($CDCl_3$) δ 3.54 (1H, q, J = 11.3 Hz), 3.37–3.21 (1H, m), 2.50 (2H, bs), 1.60–1.22 (8H, m), 1.15 (3H, d, J = 11.3 Hz), 0.85 (3H, t, J = 9.4 Hz). ^{13}C-NMR ($CDCl_3$) δ 76.2, 70.9, 33.2, 31.7, 25.1, 22.4, 19.3, 13.8. Anal. Calcd for $C_8H_{18}O_2$: C, 65.71; H, 12.41. Found: C, 65.87; H, 12.39.

(4*R,5*R**)-4,5-Decanediol (16).** A three-necked round bottom flask with a nitrogen inlet was charged with CuI (0.95 g, 5 mmol) and Et_2O (8 mL). The solution was stirred and cooled at −35 °C, and then BuLi (10 mmol, 1.6 M in hexane, 6.25 mL) was added. After 30 min compound **5** (244 mg, 1 mmol) dissolved in Et_2O (5 mL) was added. The reaction was stopped after 2 h (TLC monitoring), diluting with Et_2O and then adding saturated NH_4Cl (3 mL). The mixture was warmed to room temperature with stirring, and then the organic layer was separated. The aqueous layer was extracted with EtOAc, and the combined organic layers were washed with saturated $NaHCO_3$ (10 mL) and brine (10 mL). The organic phase was then dried over Na_2SO_4 and concentrated in vacuo. Column chromatography (hexanes/EtOAc 8:2) afforded pure compound **16** (156 mg, 90%). ^{1}H-NMR ($CDCl_3$) δ 3.51–3.22 (2H, m), 2.65 (bs, 2H), 1.65–1.05 (12H, m), 1.01–0.72 (6H, m). ^{13}C-NMR ($CDCl_3$) δ 74.4, 74.1, 35.4, 33.2, 31.7, 25.1, 22.4, 18.6, 13.83, 13.80. Anal. Calcd for $C_{10}H_{22}O_2$: C, 68.92; H, 12.72. Found: C, 68.77; H, 12.73.

(2*R,3*R**)-1-Phenyl-2,3-hexanediol (17).** A three-necked round bottom flask with a nitrogen inlet was charged with CuI (0.952 g, 5 mmol) and Et_2O (8 mL). The solution was stirred and cooled at 0 °C, and then PhLi (10 mmol, 1.6 M in hexane, 6.25 mL) was added. After 30 min compound **5** (244 mg, 1 mmol), dissolved in Et_2O (5 mL), was added and the temperature was raised to room temperature. The reaction was stopped after 2 h (TLC monitoring), diluting with Et_2O and then adding saturated NH_4Cl (3 mL). The mixture was stirred at rt, and then the organic layer was separated. The aqueous layer was extracted with EtOAc, and the combined organic layers were washed with saturated $NaHCO_3$ (10 mL) and brine (10 mL). The organic phase was then dried over Na_2SO_4 and concentrated in vacuo. Column chromatography (hexanes/EtOAc, 8:2) afforded pure compound **17** (184 mg, 95%). ^{1}H-NMR ($CDCl_3$) δ 7.48–7.07 (5H, m), 3.68–3.55 (1H, m) 3.51–3.40 (1H, m) 2.87 (1H, dd, J = 13.4, 8.3 Hz), 2.68 (1H, dd, J = 13.4, 8.3 Hz), 2.28 (2H, bs), 1.60–1.25 (4H, m), 0.93 (3H, t, J = 7.4 Hz). ^{13}C-NMR ($CDCl_3$) δ 138.4, 129.5, 128.74, 128.69, 128.6, 126.6, 74.9, 73.1, 40.0, 35.6, 18.6, 13.8. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.14; H, 9.32.

(4*R,5*R**)-7-Nonen-4,5-diol (18)** (mixture of cis and trans isomers). To a three-necked round bottom flask equipped with a magnetic apparatus and a nitrogen inlet was added Li (365 mg, 52 mmol) in Et_2O (8 mL). The solution was cooled at −10 °C, and 1-bromopropene (1 mL, 15 mmol) dissolved in Et_2O (4 mL) was added. After 2 h the reaction mixture was warmed to rt and left for 1 h. The prepared lithium propene (240 mg, 5 mmol) was slowly added via cannula at −78 °C to a two-necked round bottom flask with a nitrogen inlet that was charged with CuI (476 mg, 2.5 mmol) dissolved in Et_2O (3 mL). The reaction mixture stood at −35 °C, and then compound **5** (122 mg, 0.5 mmol) diluted in Et_2O (2 mL) was added. The reaction was stopped after 24 h (TLC monitoring) and quenched with saturated NH_4Cl (3 mL). The aqueous layer was then extracted with EtOAc (50 mL), and the organic phases were dried over Na_2SO_4 and concentrated in vacuo. Column chromatography (hexanes/EtOAc 7:3) afforded pure compound **18** (73 mg, 92%). ^{1}H-NMR ($CDCl_3$) δ 5.71–5.30 (2H, m), 3.70–3.30 (2H, m), 2.48 (2H, bs), 2.31–2.05 (2H, m), 1.64 (3H, d, J = 6.0 Hz), 1.55–1.25 (4H, m), 0.91 (3H, t, J = 7.4 Hz). ^{13}C-NMR ($CDCl_3$) δ 129.6, 127.3, 126.9, 125.8, 73.9, 73.5, 37.1, 35.5, 35.4, 32.8, 31.1, 18.6, 18.0, 13.8, 12.3. Anal. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.47. Found: C, 68.27; H, 11.46.

(4*R,5*R**)-5-Hydroxy-4-octanolide (19).** To a two-necked round bottom flask equipped with a magnetic stirrer, a nitrogen inlet, and a condenser was added Na (23 mg, 1 mmol) in EtOH (3 mL). Then, diethyl malonate (228 mg, 1.8 mmol) was added and the temperature was raised to reflux. Compound **5** (70 mg, 0.3 mmol) was then added, and the reaction was continued for 1 h (TLC monitoring). Water was then added to the reaction mixture (1 mL), and the solvents were evaporated in vacuo. Dilution with Et_2O was followed by extraction with brine: the organic layer was then dried over Na_2SO_4 and concentrated in vacuo. NaOH (2 mL of 2 N solution) was then added to the residue, and the resulting mixture was refluxed for 1.5 h. Then H_2SO_4 (2 mL) in water (3 mL) was added, and reflux was continued for 18 h. After cooling the reaction mixture, Et_2O (10 mL) was added and the organic layer was washed ($NaHCO_3$ and brine), dried over Na_2SO_4, and concentrated in vacuo. Column chromatography (hexanes/EtOAc 6:4) afforded pure compound **19** (28 mg, 60%). ^{1}H-NMR ($CDCl_3$) δ 4.45–4.32 (1H, m), 3.65–3.50 (1H, m), 2.65–2.48 (2H, m), 2.35–2.02 (2H, m), 1.87 (1H, bs), 1.65–1.32 (4H, m), 0.92 (3H, t, J = 6.5 Hz). ^{13}C-NMR ($CDCl_3$) δ 177.3, 82.9, 73.3, 34.9, 28.5, 23.9, 18.5, 13.7. Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.77; H, 8.99.

(2*E*)-Ethyl-2-pentadecenoate (21). To a two-necked round bottom flask equipped with a condenser and stirring apparatus was added, under an argon atmosphere, commercially available tridecanal **20** (2 g, 10 mmol) dissolved in THF (100 mL), followed by LiOH (0.462 g, 11 mmol) and triethyl phosphonacetate (2.5 g, 11 mmol). The reaction mixture was refluxed for 2 h (TLC monitoring) and then quenched with water (15 mL). The mixture was then extracted with EtOAc (50 mL), and the organic phase was dried over Na_2SO_4 and concentrated in vacuo. Column chromatography (hexanes/EtOAc 9:1) afforded pure compound **21** (2.5 g, 90%). ^{1}H-NMR ($CDCl_3$) δ 7.05–6.86 (1H, m), 5.79 (1H, dt, J = 16.7, 1.5 Hz), 4.18 (2H, q, J = 7.1 Hz), 2.23–2.09 (2H, m), 1.47–1.13 (23H, m), 0.85 (3H, t, J = 5.9). ^{13}C-NMR ($CDCl_3$) δ 166.7,149.4, 121.2, 59.8, 31.9, 31.6, 29.3, 29.2, 29.1,28.9, 27.7, 22.4, 13.9, 13.7. Anal. Calcd for $C_{17}H_{32}O_2$: C, 76.06; H, 12.02. Found: C, 76.11; H, 11.98.

(2*E*)-2-Pentadecen-1-ol (22). To a solution of compound **21** (1.2 g, 4.5 mmol) in toluene (100 mL), under a nitrogen atmosphere and with stirring, was slowly added DIBAL (9 mL of a 1 M solution in toluene, 9 mmol). After 1 h (TLC monitoring), the reaction was quenched with saturated NH_4Cl (20 mL) and the mixture was extracted with Et_2O (100 mL): the organic layer was then dried over Na_2SO_4 and concentrated in vacuo, affording crude compound **22** (0.927 g, 91%). ^{1}H-NMR ($CDCl_3$) δ 5.68–5.55 (2H, m), 4.04 (2H, d, J = 5.3 Hz), 2.08–1.87 (2H, m), 1.42–1.11 (21H, m), 0.85 (3H, bt, J = 6.0 Hz). ^{13}C-NMR ($CDCl_3$) δ 133.6, 128.9, 63.6, 32.0, 31.7, 29.5, 29.3, 29.2, 29.0, 28.97, 22.5, 13.9. Anal. Calcd for $C_{15}H_{30}O$: C, 79.58; H, 13.36. Found: C, 79.61; H, 13.34.

(2*R*,3*R*)-2,3-Epoxypentadecan-1-ol (23). The AE was performed on compound **22** (460 mg, 2.0 mmol), with D-(−)-DET as chiral auxiliary (as described before for compound **15**) to afford after column chromatography (hexenes/EtOAc 7:3) compound **23** (452 mg, 89%). $[\alpha]_D = +21°$ (*c* 1.57, $CHCl_3$), ee > 97% (determined via Mosher derivative). ^{1}H-NMR ($CDCl_3$) δ 3.81 (1H, dd, J = 12.3, 2.8 Hz), 3.51 (1H, dd, J =12.3, 4.0 Hz), 2.93–2.80 (2H, m), 2.60 (1H, bt, J = 6.3 Hz), 1.58–1.14 (22H, m), 0.82 (3H, t, J = 7.0 Hz). ^{13}C-NMR ($CDCl_3$) δ 61.7, 58.5, 56.0, 31.7, 31.3, 29.4, 29.3, 29.2, 29.1, 25.7, 22.4, 13.8.

Anal. Calcd for $C_{15}H_{30}O_2$: C, 74.32; H, 12.47. Found: C, 74.36; H, 12.41.

(2*R*,3*R*)-1-Iodo-2,3-pentadecanediol (24). According to the general procedure compound **23** (110 mg, 0.45 mmol) afforded after column chromatography (hexanes/ether 7:3) pure compound **24** (114 mg, 70%). $[\alpha]_D$ = +3.15° (*c* 1.57, $CHCl_3$), ^{1}H-NMR ($CDCl_3$) δ 3.72−3.57 (1H, m), 3.54−3.42 (1H, m), 3.40−3.22 (2H, m), 2.52 (1H, bs), 2.05 (1H, bs), 1.65−1.09 (22H, m), 0.85 (3H, t, J = 6.9 Hz). ^{13}C-NMR ($CDCl_3$) δ 73.5, 73.0, 33.7, 31.7, 29.5, 29.4, 29.2, 25.3, 22.5, 13.9, 10.4.

(−)-(*R*,*R*)-Muricatacin. Following the procedure described for the preparation of compound **19**, compound **25** (40 mg, 0.11 mmol) afforded after column chromatography (−)-muricatacin (15 mg, 50%). $[\alpha]_D$ = −21.9° (*c* 1.57, $CHCl_3$) (lit.[17a] $[\alpha]_D$ = −23.14°. ^{1}H-NMR ($CDCl_3$) δ 4.45−4.32 (1H, m), 3.62−3.49 (1H, m), 2.65−2.48 (2H, m), 2.35−2.02 (3H, m), 1.55−1.12 (20H, m), 0.86 (3H, t, J = 6.9 Hz).

(2*R*,3*S*)-1-(Benzyloxy)-2,3-octanediol (26). The known chiral compound **25** was prepared according to ref 14 (130 mg, 0.4 mmol) and then subjected to the general procedure with LiI in DME, affording, after purification pure chiral compound **8** (76 mg, 75%). Then compound **8** was coupled with lithium dibutylcuprate, with the procedure described for compound **16**, affording after column chromatography (hexanes/EtOAc 6:4) pure chiral compound **26**. $[\alpha]_D$ = −8.9° (*c* 1.57, $CHCl_3$) (lit.[18] $[\alpha]_D$ = −8.77° (EtOH)). ^{1}H-NMR ($CDCl_3$) δ 7.33 (5H, bs), 4.52 (2H, s), 3.82−3.53 (4H, m), 2.75 (1H, d, J = 5.2 Hz), 1.5 (1H, bs), 1.55−1.05 (8H, m), 0.87 (3H, t, J = 7.2 Hz). ^{13}C-NMR ($CDCl_3$) δ 128.7, 128.1, 128.0, 73.7, 73.2, 72.5, 71.0, 32.7, 32.0, 25.4, 22.4, 13.8. Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.33; H, 9.62.

(2*R*,3*S*)-1-(Benzyloxy)-2,3-butanediol (12). The chiral compound **12** was prepared following the same procedure described for racemic compound **12**: starting from chiral compound **25** (200 mg, 1.03 mmol), the final product **12** was obtained after purification (123 mg, 62%). ^{1}H and ^{13}C-NMR are identical to those reported above for racemic compound **12**. $[\alpha]_D$ = −7.0° (*c* 1.57, EtOH) (lit.[18] $[\alpha]_D$ = −7.2° (EtOH)). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.29; H, 8.24.

(2*S,3*S**)-1-(Tosyloxy)-2,3-epoxyhexane (27).** To a two-necked round bottom flask, under argon atmosphere and with stirring, were added 2-hexen-1-ol (1 g, 10 mmol) in CH_2Cl_2 (40 mL) and $Ti(OiPr)_4$ (3.41 g, 12 mmol). The solution, cooled to −20 °C, was stirred for 30 min and then TBHP (5.33 mL of a 3 M solution in isoctane, 16 mmol) was added. After 2 h to the stirred solution was slowly added $P(OMe)_3$ (2.5 g, 20 mmol), and then Et_3N (2.5 mL, 18 mmol), DMAP (183 mg, 1.5 mmol), and TsCl (2.4 g, 12.5 mmol) were added. After 5 h, the reaction was stopped (TLC monitoring with UV lamp) and filtered on Celite eluting with CH_2Cl_2. The collected filtrate was washed with tartaric acid (10%, 10 mL) and then with $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4 and concentrated in vacuo: then the crude product was chromatographed (hexanes and then hexanes/ether 8:2) to afford compound **27** (0.8 g, 80%). ^{1}H-NMR ($CDCl_3$) δ 7.78 (2H, d, J = 8.5 Hz), 7.32 (2H, d, J = 8.5 Hz), 4.16 (1H, dd, J = 11.5, 3.8 Hz), 3.94 (1H, dd, J = 11.5, 5.8 Hz), 2.97−2.88 (1H, m), 2.81−2.70 (1H, m), 2.42 (3H, s), 1.55−1.28 (4H, m), 0.92 (3H, t, J = 7.7 Hz). ^{13}C-NMR ($CDCl_3$) δ 145.2, 132.9, 130.0, 128.1, 70.1, 56.5, 54.4, 33.1, 21.5, 18.9, 13.6. Anal. Calcd for $C_{13}H_{18}O_4S$: C, 57.76; H, 6.71. Found: C, 57.73; H, 6.72.

(2*S,3*S**)-1-(Tosyloxy)-2-methyl-2,3-epoxypentane (28).** According to the procedure described for compound **27**, (*E*)-2-methyl-2-penten-1-ol[20] (1.1 g) afforded compound **28** (0.88 g, 69%). ^{1}H-NMR ($CDCl_3$) δ 7.79 (2H, d, J = 8.3 Hz), 7.34 (2H, d, J = 8.3 Hz), 3.92 (2H, s), 2.73 (1H, t, J = 6.4 Hz), 2.44 (3H, s), 1.65−1.42 (2H, m), 1.28 (3H, s), 0.98 (3H, t, J = 7.6 Hz). ^{13}C-NMR ($CDCl_3$) δ 130.0, 128.1, 74.4, 62.7, 57.8, 21.5, 21.3, 13.7, 10.1. Anal. Calcd for $C_{13}H_{18}O_4S$: C, 57.76; H, 6.71. Found: C, 57.79; H, 6.72.

(2*S,3*S**,4*S**)-2-(Tosyloxy)-3,4-epoxypentane (29).** In a round bottom flask under a nitrogen atmosphere and with stirring, the known 3,4-epoxypentan-2-ol[12d] (0.5 g, 4.9 mmol) was dissolved in CH_2Cl_2 (8 mL) and then charged with TsCl (1.03 g, 5.4 mmol). The reaction was heated to 40 °C and stopped after 12 h (TLC monitoring) with addition of ether (10 mL). The mixture was washed with 1 N HCl (10 mL) and with brine until neutral. The organic layer was dried over Na_2SO_4 and evaporated in vacuo. Column chromatography (hexanes/EtOAc 9:1) afforded compound **29** (0.9 g, 72%). ^{1}H-NMR ($CDCl_3$) δ 7.78 (2H, d, J = 8.4 Hz), 7.30 (2H, d, J = 8.4 Hz), 4.51−4.32 (1H, m), 2.93−2.81 (1H, m), 2.74 (1H, dd, J = 5.6, 2.2 Hz), 2.41 (3H, s), 1.30 (3H, d, J = 6.7 Hz), 1.23 (3H, d, J = 5.6 Hz). ^{13}C-NMR ($CDCl_3$) δ 144.8, 134.2, 129.8, 127.8, 79.1, 59.8, 52.0, 21.4, 17.2, 16.8. Anal. Calcd for $C_{12}H_{16}O_4S$: C, 56.23; H, 6.29. Found: C, 56.28; H, 6.69.

(1*S,2*S**,3*S**)-1-(Tosyloxy)-2,3-epoxycyclohexane (30).** According to the procedure described for compound **29**, the known 2,3-epoxy-1-cyclohexanol[12d] (200 mg) afforded compound **30** (424 mg, 90%). ^{1}H-NMR ($CDCl_3$) δ 7.80 (2H, d, J = 8.4 Hz), 7.32 (2H, d, J = 8.4 Hz), 4.92−4.77 (1H, m), 3.28−3.09 (2H, m), 2.43 (3H, s), 1.91−1.04 (6H, m). ^{13}C-NMR ($CDCl_3$) δ 144.8, 134.5, 129.9, 127.7, 79.1, 54.7, 52.5, 25.1, 21.8, 21.4, 19.4. Anal. Calcd for $C_{13}H_{16}O_4S$: C, 58.19 H, 6.01. Found: C, 58.16; H, 6.03.

(3*S,4*S**)-1-(Tosyloxy)-3,4-epoxyhexane (31).** According to the procedure described for compound **29**, commercially available (*E*)-3-hexen-1-ol (200 mg) gave pure compound **31** (330 mg, 72%). ^{1}H-NMR ($CDCl_3$) δ 7.73 (2H, d, J = 9.0 Hz), 7.29 (2H, d, J = 9.0 Hz), 4.19 (2H, t, J = 5.8), 2.73−2.55 (2H, m), 2.39 (3H, s), 1.95−1.62 (2H, m), 1.60−1.35 (2H, m), 0.89 (3H, t, J = 6.8 Hz). ^{13}C-NMR ($CDCl_3$) δ 145.0, 132.9, 129.9, 127.9, 67.2, 59.6, 54.3, 31.5, 24.5, 21.3, 9.3. Anal. Calcd for $C_{13}H_{18}O_4S$: C, 57.76; H, 6.71. Found: C, 57.72; H, 6.73.

General Preparation of Tosylhalohydrins with LiX: Representative Procedure for the Preparation of (2*R,3*S**)-1-(Tosyloxy)-3-iodohexan-2-ol (32).** Compound **27** (270 mg, 1 mmol) was dissolved with magnetic stirring in CH_3CN (10 mL, used as purchased) in a round bottom flask. To the solution were added the resin Amberlyst 15 (27 mg, 1 mmol) and LiI (134 mg, 1 mmol). After the reaction was completed (TLC monitoring), the mixture was diluted with AcOEt and filtered on paper. The collected filtrate was washed with $Na_2S_2O_3$ (5 mL), dried over Na_2SO_4, and concentrated in vacuo. The crude product was analyzed, before purification, to determine the regioisomeric ratio (^{1}H and ^{13}C-NMR). Column chromatography (hexanes/EtOAc 8:2) afforded pure compound **32** (394 mg, 99%). ^{1}H-NMR ($CDCl_3$) δ 7.78 (2H, d, J = 9.0 Hz), 7.33 (2H, d, J = 9.0 Hz), 4.30 (1H, dd, J = 10.0, 4.0 Hz), 4.21−4.0 (2H, m), 3.82−3.67 (1H, m), 2.55 (1H, bs), 2.42 (3H, s), 1.87−1.16 (4H, m), 0.87 (3H, t, J = 8.0 Hz). ^{13}C-NMR ($CDCl_3$) δ 145.4, 132.4, 130.0, 128.0, 72.8, 72.7, 37.8, 36.7, 22.5, 21.4, 12.8.

(2*R,3*S**)-1-(Tosyloxy)-3-bromohexan-2-ol (33).** According to the general procedure with LiBr, compound **27** (50 mg) afforded compound **33** (63 mg, 99%). ^{1}H-NMR ($CDCl_3$) δ 7.79 (2H, d, J = 8.6 Hz), 7.34 (2H, d, J = 8.6 Hz), 4.29 (1H, dd, J = 11.5, 3.8 Hz), 4.15 (1H, dd, J = 11.5, 5.7 Hz), 4.05−3.85 (2H, m), 2.57 (1H, bs), 2.42 (3H, s), 1.99−1.12 (4H, m), 0.88 (3H, t, J = 6.7 Hz). ^{13}C-NMR ($CDCl_3$) δ 145.4, 130.1, 128.1, 72.3, 71.5, 56.2, 35.6, 21.4, 20.3, 13.0.

(2*R,3*S**)-1-(Tosyloxy)-3-chlorohexan-2-ol (34).** According to the general procedure with LiCl, compound **27** (50 mg) afforded compound **34** (55 mg, 99%). ^{1}H-NMR ($CDCl_3$) δ 7.78 (2H, d, J = 7.8 Hz), 7.33 (2H, d, J = 7.8 Hz), 4.27 (1H, dd, J = 7.8, 2.7 Hz), 4.18−4.0 (2H, m), 3.93−3.79 (2H, m), 2.41 (3H, s), 1.87−1.24 (4H, m), 0.87 (3H, t, J = 6.4 Hz). ^{13}C-NMR ($CDCl_3$) δ 145.4, 132.5, 130.1, 128.1, 72.3, 71.0, 62.1, 35.3, 21.4, 19.1, 13.2. Anal. Calcd for $C_{13}H_{19}O_4$ Cl S: C, 50.89; H, 6.24. Found: C, 50.86; H, 6.25.

(2*R,3*S**)-1-(Tosyloxy)-2-methyl-3-iodopentan-2-ol (35).** According to the general procedure with LiI, compound **28** (100 mg) afforded compound **35** (146 mg, 99%). ^{1}H-NMR ($CDCl_3$) δ 7.78 (2H, d, J = 8.5 Hz), 7.33 (2H, d, J = 8.5 Hz), 4.18 (1H, d, J = 11.3 Hz), 4.10 (1H, d, J = 11.3), 3.92 (1H, dd, J = 11.3, 3.8 Hz), 2.53 (1H, bs), 2.42 (3H, s), 1.98−1.50 (2H, m), 1.29 (3H,s), 0.98 (3H, t, J = 6.6 Hz). ^{13}C-NMR ($CDCl_3$) δ 145.4, 132.2, 130.1, 128.2, 76.0, 73.2, 46.1, 27.0, 20.4, 14.9.

(2*S,3*S**,4*R**)-2-(Tosyloxy)-4-iodopentan-3-ol (36).** According to the general procedure with LiI, compound **29** (30 mg) afforded compound **36** (44 mg, 99%). ^{1}H-NMR ($CDCl_3$) δ

7.80 (2H, d, J = 8.7 Hz), 7.35 (2H, d, J = 8.7 Hz), 4.15–3.98 (2H, m), 3.60 (1H, dd, J = 7.4, 3.0 Hz), 2.44 (3H, s), 2.25–2.35 (1H, bs), 1.93 (3H, d, J = 7.4 Hz), 1.35 (3H, d, J = 6.5 Hz).

(1*S,2*R**,3*R**)-1-(Tosyloxy)-3-Iodocyclohexan-2-ol (37).** According to the general procedure with LiI, compound **30** (70 mg) afforded compound **37** (101 mg, 99%). ^{1}H-NMR ($CDCl_3$) δ 7.80 (2H, d, J = 8.7 Hz), 7.32 (2H, d, J = 8.7 Hz), 4.98–4.84 (1H, m), 4.31–4.12 (1H, m), 3.68 (1H, dd, J = 8.7, 3.9 Hz), 2.65 (1H, bs), 2.42 (3H, s), 2.30–1.10 (6H, m). ^{13}C-NMR ($CDCl_3$) δ 145.1, 133.7, 130.0, 128.0, 79.8, 74.5, 35.0, 32.3, 28.6, 21.5, 21.2.

(1*S,2*R**,3*R**)-1-(Tosyloxy)-3-bromocyclohexan-2-ol (38).** According to the general procedure with LiBr, compound **30** (50 mg) afforded compound **38** (85 mg, 99%). ^{1}H-NMR ($CDCl_3$) δ 7.81 (2H, d, J = 9.1 Hz), 7.32 (2H, d, J = 9.1 Hz), 4.96–4.86 (1H, m), 4.22–4.03 (1H, m), 3.70 (1H, dd, J = 9.1, 3.6 Hz), 2.57 (1H, bs), 2.42 (3H, s), 2.72–1.33 (6H, m). ^{13}C-NMR ($CDCl_3$) δ 145.1, 130.0, 128.1, 80.3, 73.8, 53.4, 32.9, 28.4, 21.5, 19.9.

(1*S,2*R**,3*R**)-1-(Tosyloxy)-3-chlorocyclohexan-2-ol (39).** According to the general procedure with LiCl, compound **30** (50 mg) afforded compound **39** (66 mg, 92%). ^{1}H-NMR ($CDCl_3$) δ 7.80 (2H, d, J = 9.2 Hz), 7.32 (2H, d, J = 9.2 Hz), 4.97–4.85 (1H, m), 4.16–3.98 (1H, m), 3.64 (1H, dd, J = 8.9, 3.6 Hz), 2.42 (4H, s), 2.26–1.39 (6H, m). ^{13}C-NMR ($CDCl_3$) δ 145.1, 130.0, 128.1, 80.4, 73.8, 60.6, 31.9, 28.2, 21.5, 19.0.

(3*S,4*R**)-1-(Tosyloxy)-4-iodohexan-3-ol (40).** According to the general procedure with LiI, compound **31** (100 mg) afforded compound **40** (132 mg, 90%). ^{1}H-NMR ($CDCl_3$) δ 7.79 (2H, d, J = 8.0 Hz), 7.33 (2H, d, J = 8.0 Hz), 4.24–4.02 (3H, m), 3.42–3.29 (1H, m), 2.58 (1H, bs), 2.42 (3H, s), 2.16–1.18 (4H, m), 0.90 (3H, t, J = 6.0 Hz). ^{13}C-NMR ($CDCl_3$) δ 145.1, 132.9, 130.0, 128.0, 70.4, 67.2, 49.8, 34.1, 28.3, 21.5, 14.4.

(3*S,4*R**)-1-(Tosyloxy)-4-bromohexan-3-ol (41).** According to the general procedure with LiBr, compound **31** (50 mg) afforded compound **41** (35 mg, 55%). ^{1}H-NMR ($CDCl_3$) δ 7.79 (2H, d, J = 7.6 Hz), 7.35 (2H, d, J = 7.6 Hz), 4.33–4.12 (2H, m), 4.11–3.97 (1H, m), 3.87–3.72 (1H, m) 2.44 (3H, s), 2.18–1.48 (5H, m), 1.05 (3H, t, J = 7.6 Hz). ^{13}C-NMR ($CDCl_3$) δ 145.1, 130.0, 128.1, 70.3, 67.3, 65.6, 32.6, 29.5, 26.8,21.5, 12.3.

(3*S,4*R**)-1-(Tosyloxy)-4-chlorohexan-3-ol (42).** According to the general procedure with LiCl, compound **31** (50 mg) afforded compound **42** (50 mg, 90%). ^{1}H-NMR ($CDCl_3$) δ 7.79 (2H, d, J = 8.9 Hz), 7.35 (2H, d, J = 8.9 Hz), 4.30–4.12 (2H, m), 3.93–3.80 (2H, m), 2.42 (3H, s), 2.20–1.42 (4H, m), 1.10 (3H, t, J = 7.3 Hz). ^{13}C-NMR ($CDCl_3$) δ 145.1, 130.0, 128.0, 70.3, 69.7, 67.4, 31.7, 26.2, 21.6, 11.0.

1-(Tosyloxy)hexan-2-ol (43). To a solution of compound **32** (200 mg, 0.5 mmol) in dry toluene (5 mL) were added AIBN (catalytic amount, 10 mg) and Bu_3SnH (112 mg, 0.41 mmol), and the temperature was raised to 70 °C. After 1 h (TLC monitoring with UV lamp), the reaction was stopped and most of the solvents were evaporated. The concentrate was diluted with CH_3CN (50 mL) and washed with hexane (5 mL, three times) to remove most of the tin residues. The solvent was evaporated in vacuo affording a crude mixture which was then chromatographed on silica gel (hexanes/ether 9:1) to pure compound **43** as colorless oil (91 mg, 82%). ^{1}H-NMR ($CDCl_3$) δ 7.79 (2H, d, J = 8.3 Hz), 7.35 (2H, d, J = 8.3 Hz), 4.06–3.75 (3H, m), 2.42 (3H, s), 2.05 (1H, bs), 1.78–1.12 (6H, m), 0.90 (3H, t, J = 6.8 Hz). ^{13}C-NMR ($CDCl_3$) δ 145.4, 130.0, 128.0, 73.9, 69.2, 32.1, 27.1, 22.2, 21.3, 13.6. Anal. Calcd for $C_{13}H_{20}O_4S$: C, 57.33; H, 7.4. Found: C, 57.28; H, 7.2.

General Preparation of 1-(Tosyloxy)-2-alkanols with MgI_2 and Bu_3SnH: Representative Procedure for the Preparation of 1-(Tosyloxy)butan-2-ol (45). Known 1-(tosyloxy)-2,3-epoxybutane **44**[14] (315 mg, 1.3 mmol) was dissolved in toluene (10 mL) and cooled at −60 °C with vigorous stirring under nitrogen. Then MgI_2 (0.65 mmol) in ether (1.3 mL) was added. After the appropriate time (TLC monitoring) the reaction mixture was allowed to warm to rt. AIBN (catalytic amount, 10 mg) and Bu_3SnH (416 mg, 1.4 mmol) were added, and the temperature was raised to 70 °C. After 1 h, the reaction was stopped and most of the solvents were evaporated. The concentrate was diluted with CH_3CN (50 mL) and washed with hexane (5 mL, three times) to remove most of the tin residues. The solvent was evaporated in vacuo, affording a crude mixture which was then chromatographed on silica gel (hexanes/ether 9:1) to afford pure compound **45** (263 mg, 83%). ^{1}H-NMR ($CDCl_3$) δ 7.77 (2H, d, J = 8.2 Hz), 7.33 (2H, d, J = 8.2 Hz), 4.01 (1H, dd, J = 9.2, 3.7 Hz), 3.87 (1H, dd, J = 9.2, 7.3 Hz), 3.81–3.65 (1H, m), 2.43 (3H, s), 2.35 (1H, bs), 1.53–1.33 (2H, m), 0.90 (3H, t, J = 6.4 Hz). ^{13}C-NMR ($CDCl_3$) δ 145.1, 133.1, 130.0, 128.0, 73.5, 70.6, 25.6, 21.4, 9.3. Anal. Calcd for $C_{11}H_{16}O_4S$: C, 54.08; H, 6.6. Found: C, 54.18; H, 6.4.

1-(Tosyloxy)-2-methylpentan-2-ol (46). According to the general procedure with MgI_2 (see above), compound **28** (250 mg) afforded pure compound **46** (101 mg, 40%). ^{1}H-NMR ($CDCl_3$) δ 7.79 (2H, d, J = 7.6 Hz), 7.37 (2H, d, J = 7.6 Hz), 3.92 (2H, s), 2.45 (3H, s), 1.28 (3H, s), 1.55–1.20 (5H, m), 0.92 (3H, t, J = 6.3 Hz). ^{13}C-NMR ($CDCl_3$) δ 145.1, 132.5, 130.0, 128.1, 74.4, 62.8, 29.0, 26.5, 21.2, 16.2, 13.4. Anal. Calcd for $C_{13}H_{20}O_4$ S: C, 57.33; H, 7.4. Found: C, 57.26; H, 7.1.

(4*S,5*S**)-Methyl-4,5-epoxy-6-(tosyloxy)hexanoate (47).** Compound **2** (140 mg, 1 mmol) was tosylated as described for compound **29**. The crude tosylate (200 mg) was then ozonized in CH_2Cl_2 (26 mL) at −78 °C, affording after usual reductive workup (Zn, CH_3COOH) the corresponding aldehyde. This aldehyde (170 mg) was then oxidized ($RuCl_3$ hydrate, $NaIO_4$ in CH_3CN, CCl_4, and phosphate buffer) to the corresponding C_6 acid, which was immediately methylated (CH_2N_2) to the final compound. Column chromatography purification (hexanes/EtOAc 6:4) afforded pure compound **47** (60 mg, 31% overall yield from **2**). ^{1}H-NMR ($CDCl_3$) δ 7.78 (2H, d, J = 8.4 Hz), 7.32 (2H, d, J = 8.4 Hz), 4.14 (1H, dd, J = 11.4, 3.8 Hz), 3.92 (1H, dd, J = 11.4, 5.7 Hz), 3.64 (3H, s), 3.01–2.92 (1H, m), 2.89–2.79 (1H, m), 2.42 (3H, s), 2.38 (2H, t, J = 8.4 Hz), 2.04–1.82 (1H, m), 1.81–1.57 (1H, m). ^{13}C-NMR ($CDCl_3$) δ 173.1, 145.2, 132.9, 130.0, 128.0, 69.7 55.4, 54.6, 51.6, 29.7, 26.3, 21.4. Anal. Calcd for $C_{14}H_{18}O_5$ S: C, 56.36; H, 6.09. Found: C, 56.18; H, 6.2.

(5*S)-Methyl-5-hydroxy-6-(tosyloxy)hexanoate (49).** According to the general procedure with LiI compound **47** (50 mg) afforded crude compound **48**, which was then reduced with Bu_3SnH (32 mg, 0.011 mmol) and AIBN (catalytic amount) in benzene (5 mL). After 1 h at reflux, the reaction was stopped and the tin residues were removed as previously described. Finally column chromatography (hexanes/EtOAc 6:4) gave pure compound **49** (42 mg, 85%). ^{1}H-NMR ($CDCl_3$) δ 7.77 (2H, d, J = 8.1 Hz), 7.33 (2H, d, J = 8.1 Hz), 4.15–3.72 (3H, m), 3.63 (3H, s), 2.46 (3H, s), 2.31 (2H, t, J = 6.7 Hz), 1.90–1.26 (5H, m). ^{13}C-NMR ($CDCl_3$) δ 174.1, 145.3, 133.7, 130.1, 128.1, 73.7, 68.9, 51.5, 33.4, 31.8, 21.5, 20.0. Anal. Calcd for $C_{14}H_{20}O_6S$: C, 53.15; H, 6.37. Found: C, 53.19; H, 6.35.

Decan-5-ol (50). According to the procedure described for the reaction of Bu_2CuLi with compound **5**, compound **43** (70 mg) was reacted with Bu_2CuLi, affording after column chromatography (hexanes/EtOAc 9:1) pure compound **50** (30 mg, 78%). ^{1}H-NMR ($CDCl_3$) δ 3.57 (1H, bs), 1.53 (1H, bs), 1.48–1.18 (14H, m), 0.87 (6H, bt). Anal. Calcd for $C_{10}H_{22}O$: C, 75.88; H, 14.01. Found: C, 75.82; H, 14.04.

1-Phenylhexan-2-ol (51). According to the procedure described for the reaction of Ph_2CuLi with compound **5**, compound **43** (100 mg) was reacted with Ph_2CuLi, affording after column chromatography (hexanes/EtOAc 8:2) pure compound **51** (57 mg, 87%). ^{1}H-NMR ($CDCl_3$) δ 7.25 (5H, m), 3.84 (1H, m), 2.84 (1H, dd, J = 14.8, 6.7 Hz), 2.63 (1H, dd, J = 14.8, 8.9 Hz), 1.80–1.15 (7H, m), 0.91 (3H, t, J = 5.8 Hz). ^{13}C-NMR ($CDCl_3$) δ 138.7, 129.5, 128.6, 126.5, 72.8, 43.8, 36.3, 27.7, 22.5, 13.8. Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.80; H, 10.21.

2-Nonen-5-ol (52) (mixture of cis and trans isomers). According to the procedure described for the reaction of allylcuprate with compound **5**, compound **43** (100 mg) was reacted with allylcuprate, affording after column chromatography (hexanes/EtOAc 8:2) compound **52** (mixture of isomers, 40 mg, 85%). ^{1}H-NMR ($CDCl_3$) δ 5.71–5.31 (2H, m), 3.68–3.50 (1H, m), 2.28–1.94 (2H, m), 1.71–1.53 (4H, m), 1.52–1.19 (6H, m), 0.98 (3H, t, J = 6.5 Hz). ^{13}C-NMR ($CDCl_3$) δ 129.0, 127.3, 126.3 71.3, 71.0, 40.5, 36.3, 36.2, 34.8, 27.74,

27.70, 22.5, 17.8, 13.8, 12.8. Anal. Calcd for $C_9H_{18}O$: C, 76.0; H, 12.76. Found: C, 76.09; H, 12.74.

(2*R*)-1-(Tosyloxy)butan-2-ol (54). According to the procedure described for compound **45**, known (2*R*,3*R*)-1-(tosyloxy)-2,3-epoxybutane **53**[14] (0.98 g, ee > 98%, determined via Mosher derivative) afforded pure compound **54** (0.83 g, 85%). Optically active compound **54** has spectroscopic data identical to that already reported for compound **45** (see above). Anal. Calcd for $C_{11}H_{16}O_4S$: C, 54.08; H, 6.6. Found: C, 54.03; H, 6.69.

3(*R*)-Octanol. According to the procedure described for compound **50**, compound **54** (0.3 g, 1.2 mmol) was reacted with Bu_2CuLi, affording, after column chromatography (hexanes/EtOAc 9:1), pure 3(*R*)-octanol (126 mg, 81%). $[\alpha]_D = -12.5°$ (*c* 1.29, $CHCl_3$) (lit.[27] $[\alpha]_D = -9.7°$). ^{1}H-NMR ($CDCl_3$) δ 3.59–3.42 (1H, m), 1.63–1.12 (11H, m), 1.0–0.74 (6H,m). ^{13}C-NMR ($CDCl_3$) δ 73.3, 36.8, 31.7, 29.9, 25.1, 22.4, 13.8, 9.6. Anal. Calcd for $C_8H_{18}O$: C, 73.78; H, 13.93. Found: C, 73.71; H, 14.02.

(2*R*,3*R*)-1-(Tosyloxy)-2,3-epoxydecane (55). According to the AE procedure described for compound **27** (*E*)-2-decen-1-ol[14] (0.7 g, 4.5 mmol) was reacted, affording, after silica gel purification (hexanes/EtOAc 8:2), compound **55** (1.3 g, 89%, ee > 96%, determined via Eu(hfc)$_3$ ^{1}H-NMR analysis). $[\alpha]_D = +30.7°$ (*c* 1.17, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ 7.76 (2H, d, J = 8.4 Hz), 7.31 (2H, d, J = 8.4 Hz), 4.15 (1H, dd, J = 11.5, 3.8 Hz), 3.92 (1H, dd, J = 11.5, 6.8 Hz), 2.96–2.84 (1H, m), 2.78–2.68 (1H, m), 2.40 (3H, s), 1.56–1.12 (12H, m), 0.83 (3H, t, J = 7.6 Hz). ^{13}C-NMR ($CDCl_3$) δ 145.1, 130.0, 128.0, 70.1, 56.6, 54.4, 31.5, 31.0, 29.0, 28.8, 25.5, 22.3, 21.4, 13.7. Anal. Calcd for $C_{17}H_{26}O_4S$: C, 62.55; H, 8.03. Found: C, 62.65; H, 7.94.

(2*R*,3*S*)-1-(Tosyloxy)-3-iododecan-2-ol (56). According to the general procedure with LiI, compound **55** (206 mg, 0.63 mmol) was reacted with LiI, affording compound **56** (289 mg, 98%). ^{1}H-NMR ($CDCl_3$) δ 7.79 (2H, d, J = 8.9 Hz), 7.34 (2H, d, J = 8.9 Hz), 4.29 (1H, dd, J = 11.9, 4.0 Hz), 4.22–3.99 (2H, m), 3.82–3.65 (1H, m), 2.78 (1H, d, J = 5.9 Hz), 2.42 (3H, s), 1.97–1.08 (12H, m), 0.84 (3H, t, J = 5.9 Hz). ^{13}C-NMR ($CDCl_3$) δ 145.4, 132.5, 130.1, 128.1, 72.9, 72.7, 38.2, 34.8, 31.5, 29.3, 28.8, 28.4, 22.3, 21.4, 13.9.

(2*R*,3*S*)-1-(Tosyloxy)dodecan-2-ol (57). Following the procedure described for the preparation of compound **27**, (see above) compound **56** (280 mg, 0.6 mmol) was reacted with Bu_3SnH, affording, after column chromatography (hexanes/EtOAc 9:1), compound **57** (165 mg, 86%). ^{1}H-NMR ($CDCl_3$) δ 7.78 (2H, d, J = 8.6 Hz), 7.33 (2H, d, J = 8.6 Hz), 4.10–3.95 (1H, m), 3.95–3.72 (2H, m), 2.42 (3H, s), 2.23 (1H, bs), 1.48–1.09 (14H, m), 0.82 (3H, bt). ^{13}C-NMR ($CDCl_3$) δ 145.1, 130.0, 128.0, 73.9, 69.4, 32.5, 31.6, 29.2, 29.0, 25.0, 22.4, 21.3, 13.8. Anal. Calcd for $C_{17}H_{28}O_4S$: C, 62.16; H, 8.59. Found: C, 62.28; H, 8.42.

(2*R*)-1-Epoxydecane (58). In a round bottom flask, compound **57** (100 mg, 0.3 mmol) was dissolved in EtOH (10 mL), and then K_2CO_3 (42 mg, 0.3 mmol) was added with vigorous stirring. After 1 h (TLC monitoring), the reaction was stopped, the reaction mixture was filtered, and the solvent was evaporated in vacuo, affording compound **58** (45 mg, 96%). ^{1}H-NMR ($CDCl_3$) δ 2.94–2.83 (1H, m), 2.72 (1H, dd, J = 4.8, 3.4 Hz), 2.43 (1H, dd, J = 4.8, 3.1 Hz), 1.65–1.28 (14H, m), 0.85 (3H, t, J = 6.4 Hz). ^{13}C-NMR ($CDCl_3$) δ 52.3, 47.0, 32.3, 31.7, 29.33, 29.28, 29.0, 25.8, 22.4, 13.8. Anal. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.9. Found: C, 76.95; H, 12.6.

(2*R,3*S**)-1,3-Diiodohexan-2-ol (59).** In a round bottom flask, under a nitrogen atmosphere, compound **27** (270 mg, 1 mmol) was dissolved in toluene (10 mL). The reaction temperature was then kept at −60 °C with vigorous stirring. Then MgI_2 (0.5 mmol) in Et_2O (1 mL) was added. After formation of the corresponding iodohydrin **32** (TLC monitoring), the temperature was raised to 25 °C and MgI_2 (0.5 mmol) in Et_2O (1 mL) was subsequently added. After 1 h the reaction was quenched with saturated $Na_2S_2O_3$ (5 mL), and then, after extraction, the organic layer was dried over Na_2SO_4 and the solvent evaporated in vacuo. The crude product was purified by column chromatography (hexanes/ether 9:1), obtaining **59** (301 mg, 85%). ^{1}H-NMR ($CDCl_3$) δ 4.26–4.12 (1H, m), 3.61–3.39 (3H, m), 2.31 (1H, bs), 1.88–1.23 (4H, m), 0.93 (3H, t, J = 8.1 Hz). ^{13}C-NMR ($CDCl_3$) δ 74.4, 41.9, 36.9, 22.7, 13.7, 12.9.

Hexan-2-ol (60). According to the procedure described for compound **43**, compound **59** (301mg) was reacted with Bu_3SnH to afford, after purification, pure compound **60** (115 mg, 96%). ^{1}H-NMR ($CDCl_3$) δ 3.51–4.0 (1H, m), 1.6–1.2 (7H, m), 1.11 (3H, d, J = 6.5 Hz), 0.95 (3H, bt, J = 6.5 Hz). ^{13}C-NMR ($CDCl_3$) δ 67.2, 39.1, 28.3, 23.4, 22.8, 13.9.

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Supporting Information Available: ^{1}H and ^{13}C-NMR spectra (84 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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