of benzaldehyde was 100%; no reaction occurred in the absence of the ruthenium catalyst). Therefore, the rate of aldehyde dimerization is significantly higher than the rate of acid chloride hydrogenolysis (see Table I for reaction times). The absence of aldehydes among the reaction products, even when the conversion of starting acid chloride was far from completion, confirms this conclusion. Another mechanism *not* involving the generation of free aldehyde should also be considered. Complex **3** (Scheme I) was proposed[9] to react with another aldehyde molecule to give acyl-alkoxo-type intermediate **4**. Reductive elimination of ester from **4** would lead to regeneration of the catalytically active ruthenium(0) species $[L_3Ru]$.

$$\underset{\mathbf{3}}{ArCORu(H)L_3} + ArCHO \rightarrow \underset{\mathbf{4}}{ArCORu(OCH_2Ar)L_3} \rightarrow ArCOOCH_2Ar + [L_3Ru]$$

A possible mechanism for the rhodium-catalyzed homogeneous Rosenmund-type reaction is probably the same as that for the hydrogenolysis of the carbon–chlorine bond in chloroarenes catalyzed by the same complex under phase-transfer or biphasic conditions.[12]

In conclusion, this research has resulted in the first examples of metal complex catalyzed homogeneous Rosenmund-type reduction and of a one-pot Rosenmund reduction and Tishchenko disproportionation reactions of acid chlorides.

Experimental Section

Spectral measurements were carried out on the following equipment: Varian XL 300 (^{1}H NMR), Bomemn MB-100 (FT-IR), and VG 5050 micromass (mass spectra) spectrometers. Melting points were determined with a Fisher-Johns apparatus. A Varian 6000 instrument was used for GLC analysis, using 3% OV-17 on Chromosorb W. Benzoyl chloride (Fisher Scientific Company) was distilled under reduced pressure prior to use. All other acid chlorides, triethylamine, 2,4,6-collidine, and triphenylphosphine were purchased from Aldrich Chemical Co. and were used as received, as were aqueous ruthenium trichloride (Johnson-Matthey) and hydrogen (Air Products). The complexes $[(Cy_3P)_2Rh(H)Cl_2]$,[12] $[(Ph_3P_3)Ru(H)Cl]$ (the aqueous $NaBH_4/C_6H_6$ procedure of Wilkinson and co-workers was used),[14] and $[(Ph_3P)_3RuCl_2]$[22] were prepared as described in the literature.

2-Napthaldehyde from 2-Naphthoyl Chloride. A mixture of 2-naphthoyl chloride (0.29 g, 1.52 mmol), benzene (2 mL), triethylamine (1.1 mL), and $[(Cy_3P)_2Rh(H)Cl_2]$ (0.075 g, 0.1 mmol) was placed in a 150-mL Schlenk tube, and the mixture was immediately degassed by two freeze–pump–thaw cycles. The Schlenk tube was purged with H_2, and the reaction mixture was vigorously stirred under H_2 at 50 °C (oil bath) for 65 h. Water (10 mL) and benzene (12 mL) were added, and the organic layer was separated, washed with water (2 × 10 mL), and subjected to rotary evaporation. The residue was chromatographed on silica gel first with pentane, to give naphthalene (0.006 g; 3.5%), mp 80–82 °C, and then with benzene, to form 0.242 g of crude 2-naphthaldehyde. The latter was purified by vacuum sublimation: yield 0.145 g (61%); mp 60–62 °C (lit.[23] mp 59–62 °C). ^{1}H NMR: δ 7.5–8.4 (m, 7 H, $C_{10}H_7$), 10.1 (s, 1 H, CHO).

The reaction of benzoyl chloride under the same conditions afforded benzaldehyde in 30% yield (GLC using internal standard).

General Procedure for the Ruthenium-Catalyzed Preparation of Esters from Acid Chlorides. A solution of toluene (2 mL), acid chloride (1 mmol), and 2,4,6-collidine (2 mmol) was placed in a 150-mL Schlenk tube. The ruthenium complex (0.05 mmol; see Table I) was added to the degassed solution, and the mixture was immediately degassed by two freeze–pump–thaw cycles. The Schlenk tube was purged with H_2, and the reaction mixture was stirred under H_2 at 55 °C (oil bath; see Table I for reaction times). Benzene (10 mL) was added, the mixture was washed with 10% HCl (2 × 5 mL), and the organic extract was concentrated by rotary evaporation. The residue was chromatographed on silica gel to give the pure ester. For C_6H_5COCl, $CH_3C_6H_4COCl$, and $CH_3OC_6H_4COCl$, the residue was dissolved in pentane, the solution was filtered through a short silica plug, and the filtrate was concentrated by rotary evaporation and dried.

Acknowledgment. We are grateful to British Petroleum and to the Natural Sciences and Engineering Research Council of Canada for support of this research.

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(23) Aldrich Chemical Company.

Optically Pure 1,3-Diols from (2*R*,4*R*)- and (2*S*,4*S*)-1,2:4,5-Diepoxypentane

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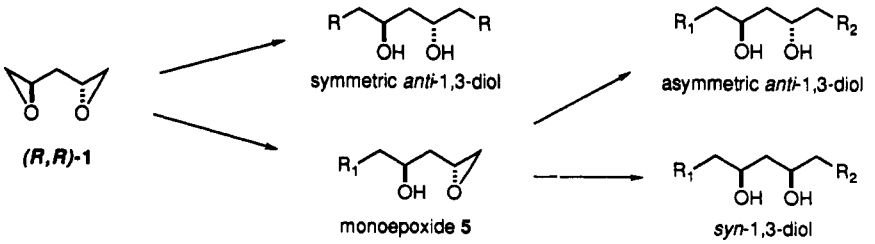
Optically pure (>97% ee) (2*R*,4*R*)-1,2:4,5-diepoxypentane (**1**) and its enantiomer can be prepared in three steps from 2,4-pentanedione without the need for chromatographic purification. Diepoxide **1** is an efficient precursor to a wide variety of optically pure syn and anti 1,3-diols. Reaction with excess nucleophile gives symmetric anti 1,3-diols in good yield. Reaction with a slight excess of alkyllithium under Ganem's conditions gives the monoepoxides **5** in good yield. Addition of a second nucleophile to monoepoxide **5** gives asymmetric anti 1,3-diols. Mitsunobu inversion of monoepoxide **5** followed by addition of a second nucleophile gives syn 1,3-diols. Optically pure syn and anti 1,3-diols are available from diepoxide **1** in one to three steps and good overall yield.



We became interested in the C_2 symmetric diepoxide **1** as a building block for 1,3-diols as part of a convergent strategy to prepare alternating polyol chains of the type found in polyene macrolide antibiotics. Our initial syn-

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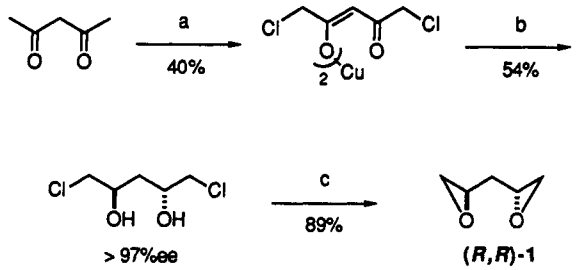
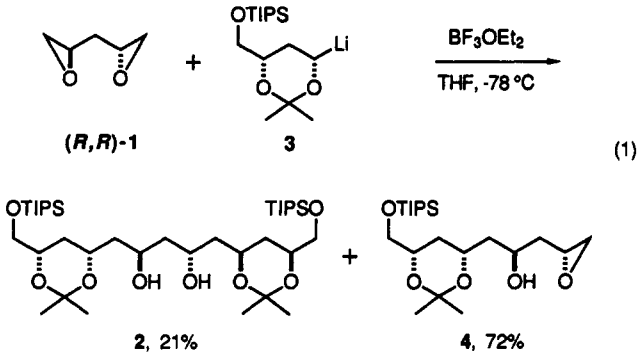
Scheme I[a]



[a] (a) $AlCl_3$, $ClCH_2C(O)Cl$, 60 °C; $Cu(OAc)_2$; (b) H_3O^+; [((S)-BINAP)$RuCl_2$]$_2Et_3N$, H_2, 1200 psi, 102 °C, MeOH; recrystallize; (c) KOH, Et_2O.

thetic target, roxaticin, could be dissected to give a C_2 symmetric tridecaneoctol with the relative stereochemistry of compound **2**, and diepoxide **1** appeared to be a particularly well-suited precursor. The coupling of optically pure alkyllithium **3**, prepared by transmetalation of the tributyltin reagent,[2] with optically pure diepoxide **1** did not proceed as expected (eq 1). Reaction of 2.2 equiv of

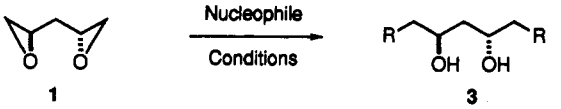


alkyllithium reagent with boron trifluoride etherate catalysis[3] gave the expected bisadduct **2** in only 21%, but the monoadduct **4** was produced in 72% yield! If the first and second alkyllithium additions proceed at equal rates, then the maximum possible yield of monoadduct would be 50%, and so one must conclude that the initial addition to give **4** is significantly faster than the second addition, which produces **2**. While this observation was disappointing with respect to the synthesis of roxaticin, it suggested that diepoxide **1** could be an effective synthetic precursor to a wide variety of symmetric and *asymmetric* optically pure 1,3-diols by the stepwise addition of alkyllithium reagents.

The 1,3-diol subunit is common to a variety of natural products and has generated much synthetic interest. A wide variety of different methods have been used to prepare stereochemically defined 1,3-diols, ranging from hydroxylation of homoallylic alcohols to 1,2-Wittig rearrangement of allylic ethers. Oishi has recently published an excellent review of the area.[4]

Diepoxides have been used in the synthesis of polyol chains.[5] The meso isomer of diepoxide **1** was used by Schreiber in his two-directional chain synthesis of syn 1,3-diols,[6,7] but because the meso isomer is achiral the optical activity was introduced in a separate enantioselective step. Diepoxide **1** has been used previously as a precursor to anti 1,3-diols. Ley used optically active diepoxide **1** as the keystone for a very efficient, convergent synthesis of the spiroketal portion of avermectin.[8] Unfortunately, his preparation of diepoxide **1** from D-ribonic acid γ-lactone required eight steps.[9] We expect that a more efficient preparation of diepoxide **1** will stimulate its use in polyol synthesis.

Table I. Symmetric Anti 1,3-Diols from Diepoxide 1[a]



nucleophile	conditions	yield, %
n-BuLi	BF_3·OEt_2, −78 °C, THF	85
$(n\text{-Bu})_2CuCNLi_2$	−78 to 0 °C, THF	84
MeLi	BF_3·OEt_2, −78 °C, THF	61
$Me_2CuCNLi_2$	−78 to 0 °C, THF	80
PhLi	BF_3·OEt_2, −78 °C, THF	94
$Ph_2CuCNLi_2$	−78 °C, THF	96
t-BuLi	BF_3·OEt_2, −78 °C, THF	18
BnLi	BF_3·OEt_2, −78 °C, Et_2O	84
CH_2=CHLi	BF_3·OEt_2, −78 °C, THF	87[b]
CH_2=$CHCH_2$Li	BF_3·OEt_2, −78 °C, Et_2O	77[c]
TMSCN	118 °C, KCN, 18-crown-6[d]	76[e]

[a] All new compounds were characterized by ^1H and ^{13}C NMR, IR, optical rotation, analysis, and/or MS. [b] 4% of the isomer from internal epoxide opening was isolated. [c] 11% of the isomer from internal epoxide opening was isolated. [d] See ref 15. [e] Isolated as the bis(TMS) ether.

We report a new synthesis of diepoxide **1** and its enantiomer in >97% ee. The key step for this preparation is an enantioselective reduction of 1,5-dichloro-2,4-pentanedione using Noyori's asymmetric hydrogenation catalyst, Scheme I.[10] 1,5-Dichloro-2,4-pentanedione was prepared from 2,4-pentanedione and isolated as its crystalline copper(II) complex.[11] Acidification and reduction with [$RuCl_2$((S)-BINAP)]$_2$–Et_3N catalysis (methanol, 102 °C, 1250 psi H_2, 60 min) gave the crude diol, which was purified by recrystallization. The (2*R*,4*R*)-1,5-dichloro-2,4-pentanediol was treated with powdered KOH in ether, filtered, and concentrated to give the diepoxide **1** as a

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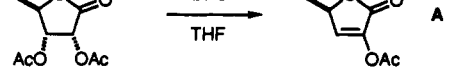
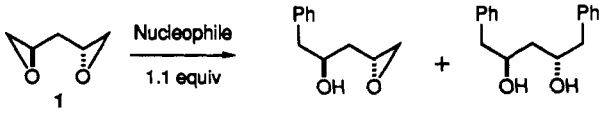
(9) The optical purity of diepoxide **1** prepared by Ley's route is 82% ee by comparison of the reported rotation ($[\alpha]_D = -47°$) and our optically pure sample. Partial racemization of enolizable intermediate **A** could have occured during elimination of the acetate by treatment with DBU: Attwood, S. V.; Barrett, A. G. M. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1315–1322.



(10) (a) Noyori, R.; Ohkuma, T.; Kitamura, M.; Takaya, H.; Sayo, N.; Kumobayashi, H.; Akutagawa, S. *J. Am. Chem. Soc.* **1987**, *109*, 5856–5858. (b) Kitamura, M.; Ohkuma, T.; Inoue, S.; Sayo, N.; Kumobayashi, H.; Akutagawa, S.; Ohta, T.; Takaya, H.; Noyori, R. *J. Am. Chem. Soc.* **1988**, *110*, 629–631. (c) Sayo, N.; Saito, T.; Kumobayashi, H.; Akutagawa, S.; Noyori, N.; Takaya, H. Eur. Pat. Appl. EP 297 752, 1987; *Chem. Abstr.* **1989**, *111*, 114745n.
(11) Matsui, K.; Motoi, M.; Nojiri, T. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 562–565.

Table II. Stoichiometric Cuprate and Alkyllithium Addition to Diepoxide 1[a]



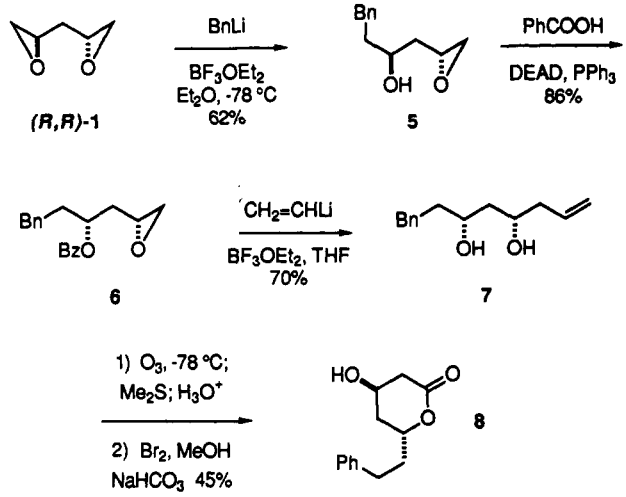
conditions	SM[a]	mono-adduct[a]	bisadduct[b]
$(Ph)_2CuCNLi_2$, THF, −78 °C	(27%)	46%	27%
PhLi, THF, BF_3·OEt_2, −78 °C	(30%)	68%	2%

[a] The amount of (volatile) starting material is estimated from the yields of monoadduct and bisadduct. [b] Isolated yields are reported for monoadduct and bisadduct.

colorless oil in 89% yield. Similarly, the enantiomer of diepoxide 1 was prepared in the same fashion, using the (*R*)-BINAP-derived catalyst. The key to this preparation is that (2*R*,4*R*)-1,5-dichloro-2,4-pentanediol is easily purified by recrystallization. The optical purity of the crude diol is only 92–94% ee by ^1H NMR analysis of the Mosher ester derivative[12] and contains a number of other impurities including the meso diol.[13] Recrystallization from dichloromethane and hexanes gives the purified diol in 64% yield from the diketone and >97% ee by NMR analysis of the Mosher ester. The diol is a stable, crystalline compound that has been stored for over a year at room temperature without decomposition. The diepoxide 1 is stable for months at 0 °C, or can be prepared in a few hours from the crystalline diol. Optically pure diepoxide 1 is available in three steps from inexpensive, commercially available precursors *without the need for chromatographic purification.*

The optically pure (>97% ee) diepoxide 1 and its enantiomer incorporate both of the stereogenic centers of the desired 1,3-diol as well as electrophilic centers suitable for coupling with a variety of carbon nucleophiles. Diepoxide 1 can be coupled with 2 equiv of the same alkyllithium reagent to give C_2 symmetric anti diols in optically pure form. Ganem's procedure using *excess* alkyllithium reagent and boron trifluoride etherate catalysis is quick and easy and gives good yields of the symmetric diols, Table I. Most alkyllithium reagents work well, including vinyl, phenyl, butyl, and benzyl, but methyllithium gives lower than average yields and *tert*-butyllithium gives significantly lower yields. The allyllithium and benzyllithium reactions are best run in ether to avoid the rapid reaction with THF under these conditions. Higher order cuprates[14] also react readily with diepoxide 1 to give symmetric anti 1,3-diols, and in difficult cases the cuprate reactions may give better results than the alkyllithium procedure, vida infra. Other nucleophiles that open epoxides will give symmetric anti 1,3-diols with diepoxide 1, as the reaction with TMSCN demonstrates.[15] Many of the optically pure, symmetric anti diols are crystalline solids that can be purified by recrystallization. These diols can in theory be prepared by asymmetric reduction of the corresponding diketone,[10] but some of these diketones are difficult to prepare and the asymmetric hydrogenation is not always selective for ketones: it will reduce alkenes and other functional groups.[16] The asymmetric reduction leading to diepoxide 1 sets the stereochemistry for this entire series of diols, and the range of symmetric anti 1,3-diols that can be prepared by this method is only limited by the choice of nucleophiles.

Scheme II



The addition of an alkyllithium reagent to diepoxide 1 catalyzed by boron trifluoride etherate proceeds in a stepwise manner with the first addition faster than the second addition and leads to a preponderance of the monoadduct, epoxy alcohol 5. This selectivity is a feature of the boron trifluoride etherate catalyzed addition of alkyllithium reagents: stoichiometric addition of a higher order cuprate reagent gives a nearly statistical mixture of the monoadduct and bisadduct, Table II. On the basis of a kinetic simulation of the product ratios, the symmetry-corrected ratio of the bimolecular rate constants for the first and second addition is approximately 0.9 for the cuprate reaction and from 6 to 12 for the alkyllithium addition. The lower rate observed in the second addition to diepoxide 1 may arise from increased steric hindrance around the epoxide, inhibiting activation by boron trifluoride. This difference in rate can be used in a practical synthesis of optically pure epoxy alcohols 5 as demonstrated in Table III. The monoadduct is the predominant product with each of the different alkyllithium reagents, but the highest selectivity is seen with phenyllithium and the lowest selectivity is found with the more reactive benzyllithium. Benzyllithium and allyllithium rapidly open THF with boron trifluoride catalysis, whereas butyllithium and phenyllithium react only slowly. The vinyllithium reaction shows good selectivity by GC, but the product is volatile and water soluble; it is more easily isolated as the *tert*-butyldimethylsilyl ether. These optically pure (>97% ee) epoxy alcohols are valuable synthetic intermediates in polyol chain synthesis.[17]

(12) Both diols were derivatized with (*R*)-Mosher's acid chloride and DMAP in CH_2Cl_2. The enantiomeric excess was determined by integration of the central CH ^1H NMR signal of each derivative at 300 MHz in $CDCl_3$: the signal for the *R,R* diol derivative appears at 2.19 ppm (dd, J = 5.3, 7.3 Hz) whereas the signal for the *S,S* diol derivative appears at 2.07 ppm (dd, J = 5.5, 7.5 Hz).

(13) Noyori reports that reduction of 1,5-dichloro-2,4-pentanedione at 30 °C produces an 87% ee, 90:10 mixture of anti:syn diols (ref 10c).

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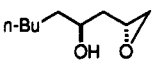
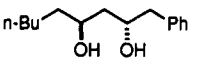
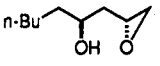
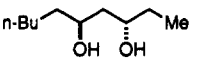
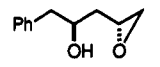
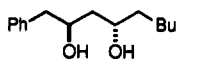
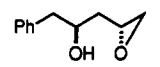
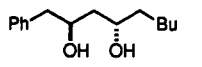
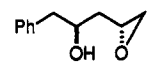
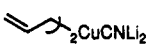
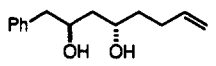
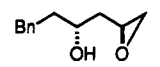
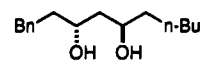
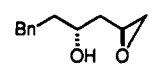
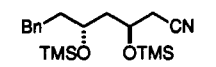
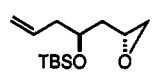
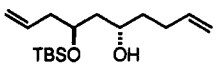
(16) Takaya, H.; Ohta, T.; Sayo, N.; Kumobayashi, H.; Akutagawa, S.; Inoue, S.-I.; Kasahara, I.; Noyori, R. *J. Am. Chem. Soc.* **1987**, *109*, 1596–1597, footnote 11.

(17) (a) Lipshutz, B. H.; Kozlowski, J. A. *J. Org. Chem.* **1984**, *49*, 1147–1149. (b) Lipshutz, B. H.; Barton, J. C. *J. Org. Chem.* **1988**, *53*, 4495–4499. (c) Lipshutz, B. H.; Kotsuki, H.; Lew, W. *Tetrahedron Lett.* **1986**, *27*, 4825–4828. (d) Mori, Y.; Kuhara, M.; Takeuchi, A.; Suzuki, M. *Tetrahedron Lett.* **1988**, *29*, 5419–5422. (e) Mori, Y.; Takeuchi, A.; Kageyama, H.; Suzuki, M. *Tetrahedron Lett.* **1988**, *29*, 5423–5426. (f) Mori, Y.; Suzuki, M. *Tetrahedron Lett.* **1989**, *30*, 4383–4386. (g) Mori, Y.; Suzuki, M. *Tetrahedron Lett.* **1989**, *30*, 4387–4388. (h) Mori, Y.; Kohchi, Y.; Suzuki, M. *J. Org. Chem.* **1991**, *56*, 631–637.

Table III. Asymmetric Anti 1,3-Diols from Diepoxide 1[a]

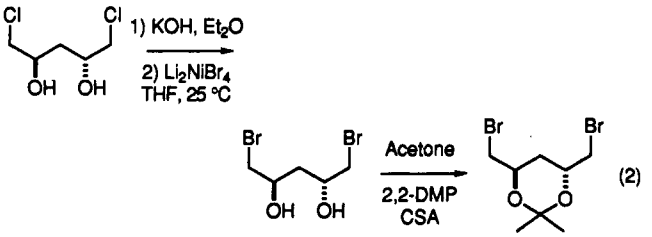
nucleophile 1	conditions	yield, %	monoadduct 5	nucleophile 2	conditions	yield, %	bisadduct
n-BuLi	$BF_3{\cdot}OEt_2$, −78 °C, THF	76		PhLi	$BF_3{\cdot}OEt_2$, −78 °C, THF	81	
				$Me_2CuCNLi_2$	−78 to 0 °C, THF	84	
PhLi	$BF_3{\cdot}OEt_2$, −78 °C, THF	79		BuLi	$BF_3{\cdot}OEt_2$, −78 °C, THF	63	
				$Bu_2CuCNLi_2$	−78 to 0 °C, THF	85	
					−78 to 0 °C, THF	81	
BnLi	$BF_3{\cdot}OEt_2$, −78 °C, THF	61		n-BuLi	$BF_3{\cdot}OEt_2$, −78 °C	80	
				TMSCN	KCN, 100 °C, 18-crown-6	89	
	(i) $BF_3{\cdot}OEt_2$, −78 °C, THF (ii) TBSCl, DMAP, CH_2Cl_2	56			$BF_3{\cdot}OEt_2$, −78 °C, Et_2O	88	

[a] All new compounds were characterized by ^1H and ^{13}C NMR, IR, analysis, MS, and optical rotation.

Epoxy alcohols **5** react with a second nucleophile to give asymmetric anti 1,3-diols as shown in Table III. Alkyllithium reagents will add to epoxy alcohols **5** with boron trifluoride etherate catalysis, but these additions are relatively slow and unreacted starting material is often observed. Higher order cuprate reagents are useful alternatives that result in higher conversions and better yields for the more difficult cases. The stepwise addition of nucleophiles to diepoxide **1** provides a very simple synthesis of a wide variety of optically pure anti 1,3-diols.

Epoxy alcohols **5** can also be used as precursors to syn diols, Scheme II. The epoxy alcohol **5**, which results from monoaddition of benzyllithium to diepoxide **1**, is a monoprotected 1,3-diol precursor, and the alcohol stereogenic center can be cleanly inverted by using the Mitsunobu procedure[18] to give the syn epoxy ester **6**. Vinyllithium addition to epoxy ester **6** cleaves the ester and adds to the epoxide to give the desired syn 1,3-diol **7** directly. Epoxy alcohols like **6** have also been produced by metal-catalyzed[19] or indirect[20] epoxidation of homoallylic alcohols to give the syn isomer, but the selectivity is variable.[21] Stepwise oxidation of alkene **7** with ozone followed by treatment with bromine in methanol gives lactone **8**, a compactin analogue[22] incorporating the pharmaceutically important lactone ring.[23] Optically pure syn 1,3-diols can be prepared in three steps from diepoxide **1**.

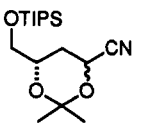
Epoxides are useful electrophiles, but alkyl halides have been used much more extensively in organic synthesis. In some situations alkyl halides are the prefered or required electrophile, as in our recently reported reductive decyanation route to polyol chains.[24] A suitable dibromo acetonide, **9**, can be prepared from diepoxide **1** in two steps (eq 2). Nucleophilic opening of the crude diepoxide **1** with



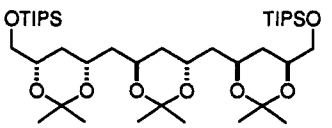
(2)

9, 79%

Li_2NiBr_4[25] and protection of the resulting free diol as an acetonide gave the desired C_2 symmetric dibromide **9** in 79% overall yield from (2*R*,4*R*)-1,5-dichloro-2,4-pentanediol. Our initial interest in diepoxide **1** as a precursor to roxaticin met with limited success, vida supra, but dibromide **9** looks to be a much more viable candidate. As previously reparted,[24] alkylation of dibromide **9** with optically pure cyanohydrin acetonide **10** followed by reductive decyanation gives the protected tridecaneoctol **11** in 58% overall yield. The relative stereochemistry of polyacetonide **11** matches that of C19–C32 of roxaticin and was confirmed by ^{13}C acetonide analysis[26] and by chemical correlation with diol **2**. Dibromide **9** will be a valuable synthon in complex polyol chain synthesis.



10



11

(18) Mitsunobu, O. *Synthesis* **1981**, 1–28.
(19) (a) Mihelich, E. D.; Daniels, K.; Eickhoff, D. J. *J. Am. Chem. Soc.* **1991**, *103*, 7690–7692. (b) Mohr, P.; Tamm, C. *Tetrahedron Lett.* **1987**, *28*, 391. (c) Reference 17a.
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Diepoxide 1 and its enantiomer were prepared by Noyori's asymmetric hydrogenation and are useful synthons for a wide variety of 1,3-diols. Symmetric and asymmetric anti 1,3-diols and syn 1,3-diols are all available in optically pure (>97% ee) form from these simple precursors.

Experimental Section

Combustion analyses were performed by M-H-W Laboratories (Phoenix, AZ). Unless otherwise noted, compounds were purified by flash chromatography[27] on E. Merck silica gel 60 (230–400 mesh), eluting with the indicated solvent system. Tetrahydrofuran and ether were distilled from benzophenone ketyl. Dichloromethane, diisopropylamine, and diethylamine were distilled from calcium hydride. Boron trifluoride etherate was distilled and stored under N_2. Air- and/or moisture-sensitive reactions were carried out under an atmosphere of nitrogen or argon using flame-dried glassware and standard syringe/septa techniques. Vinyllithium was prepared from tetravinyltin[28] and stored in a Schlenk flask at −20 °C. Benzyllithium was prepared from benzyltriphenyltin and phenyllithium in ether. The tetraphenyltin was removed by filtration and the benzyllithium solution was used immediately. Other alkyllithium reagents were purchased from Aldrich Chemical Company or prepared in situ. Higher order cuprates were prepared by the procedure of Lipschutz.[14]

Copper(II) 1,5-Dichloro-2,4-pentanedionate.[11] Aluminum chloride (80 g, 0.60 mol) was placed in a three-necked, 500-mL round-bottom flask equipped with a drying tube, a condenser, and an addition funnel. The flask was purged with N_2 followed by the addition of nitrobenzene (100 mL) and 1,2-dichloroethane (120 mL). The mixture was stirred until all of the aluminum chloride was dissolved, leaving a brown solution. 2,4-Pentanedione (61.5 mL, 0.60 mol) was then added dropwise via the addition funnel. The reaction was then cooled to 0 °C by placing the flask in an ice bath, and chloroacetyl chloride was added dropwise over a 30-min period. The reaction mixture was then removed from the ice bath and heated to 60 °C. Heating was continued until no more acetyl chloride evolved, approximately 4 h. The reaction mixture was cooled and slowly poured into a flask containing 100 mL of concd HCl and 800 g of ice followed by stirring overnight. The contents of the flask was then poured into a separatory funnel and the organic layer was removed. The aqueous layer was extracted with diethyl ether (2 × 200 mL), and the organic layers were combined and washed with H_2O (2 × 200 mL). The organic layer was then shaken with 1 L of saturated aqueous $Cu(OAc)_2$. The entire mixture was filtered through a Buchner funnel, leaving a blue-green precipitate. The aqueous portion of the filtrate was removed and the organic layer was shaken with an additional 1-L portion of $Cu(OAc)_2$ solution. This was then filtered through a Buchner funnel and the resulting blue-green precipitate was combined with the first batch. The combined solids were triturated with 100 mL of boiling diethyl ether and filtered, leaving 37.6 g of the desired product as a fine grey powder. An additional 10.5 g of product was obtained by extracting the original aqueous layer with ether (2 × 200 mL), shaking with $Cu(OAc)_2$ solution, and triturating with ether to give a combined yield 48.1 g (0.12 mol, 40%) of the previously reported product.[11]

1,5-Dichloro-2,4-pentanedione.[11] To a suspension of 11.0 g (27 mmol, 0.5 equiv) of copper(II) 1,5-dichloro-2,4-pentanedionate in 100 mL of ethyl ether was added 100 mL of 10% H_2SO_4. The reaction mixture was stirred vigourously until all the solid dissolved, approximately 45 min. The mixture was extracted (2 × Et_2O), washed (2 × brine), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude material was distilled (Kugelrohr, bp 80 °C at 1 Torr) to afford 7.65 g (45.2 mmol, 84%) of the previously reported product[11] as a clear, colorless oil, which was used in the next step without further purification.

(2R,4R)-1,5-Dichloro-2,4-pentanediol. Catalyst preparation: 39.6 mg (0.14 mmol, 1 equiv) of $RuCl_2(COD)$, 105.9 mg (0.17 mmol, 1.2 equiv) of (S)-BINAP, 234 μL (1.68 mmol, 12 equiv) of Et_3N, and 10 mL of toluene were heated at reflux for 16 h in a 100-mL Schlenk flask under N_2. The resulting orange solution was concentrated under vacuum to give crude $[RuCl_2((S)\text{-BINAP})]_2$–$Et_3N$ catalyst as an orange solid.

1,5-Dichloro-2,4-pentanedione (7.4 g, 44 mmol) was dissolved in MeOH (20 mL) and the solution was degassed with a stream of N_2. This solution was transferred via cannula to the freshly prepared $[RuCl_2((S)\text{-BINAP})]_2$–$Et_3N$ catalyst under argon. After heating the suspension to dissolve the catalyst, the orange solution was transferred to a 125-mL pressure reaction vessel (Parr no. 4751) via cannula and sealed. The reaction vessel was pressurized to 1250 psi with H_2 gas and placed in an oil bath at 102 °C. When no more hydrogen was absorbed (60 min), the reaction mixture was cooled to room temperature, concentrated under reduced pressure, and filtered thru a plug of silica gel with ether. The crude product was recrystallized (hexanes/CH_2Cl_2 2:3, v/v) to give 4.88 g (28.2 mmol, 64%) of >97% ee product as white crystals: mp 85–86 °C; $[\alpha]^{24}_D$ = +21.1° (c = 1.125, $CHCl_3$); IR (KBr) 3364, 2959, 2890, 1435, 1402, 1340, 1294, 1103, 1072, 1052, 910, 710 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6) δ 4.27 (d, J = 5.6 Hz, 1 H), 4.13–4.03 (m, 1 H), 3.65–3.52 (m, 2 H), 1.70 (dd, J = 5.5, 6.9 Hz, 1 H); ^{13}C NMR (75 MHz, acetone-d_6, DEPT) CH 68.8; CH_2 50.8, 39.6. Anal. Calcd for $C_5H_{10}Cl_2O_2$: C, 34.71; H, 5.83. Found: C, 34.67; H, 5.81.

(2R,4R)-1,2:4,5-Dianhydro-3-deoxypentitol ((R,R)-1). (2R,4R)-1,5-Dichloro-2,4-pentanediol (2.32 g, 13.4 mmol, 1 equiv) was dissolved in 100 mL of ethyl ether, the solution was cooled to 0 °C, and freshly powered KOH (5.24 g, 88.8 mmol, 6.6 equiv) was added. After being stirred for 3 h at rt, the reaction mixture was filtered through a plug of $MgSO_4$ and the ether was removed under reduced pressure from an ice bath to give 1.19 g (11.9 mmol, 89%) of the product as a colorless oil. A sample was purified by Kugelrohr distillation (bp 65 °C at 28 Torr): $[\alpha]^{25}_D$ = +57.6° (c = 2.24, $CHCl_3$): IR (neat) 3055, 2997, 2924, 1421, 1256, 980, 938, 912, 844, 792, 747 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.09–3.03 (m, 1 H), 2.78 (dd, J = 4.1, 4.9 Hz, 1 H), 2.51 (dd, J = 2.6, 4.9 Hz, 1 H), 1.72 (t, J = 5.7 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) CH 49.5; CH_2 46.9, 36.2. Anal. Calcd for $C_5H_8O_2$: C, 59.98; H, 8.05. Found: C, 60.01; H, 8.19.

(2S,4S)-1,5-Dichloro-2,4-pentanediol. The spectroscopic data matched that obtained for the enantiomer: $[\alpha]^{24}_D$ = −20.8° (c = 0.99, $CHCl_3$). Anal. Calcd for $C_5H_{10}Cl_2O_2$: C, 34.71; H, 5.83. Found: C, 34.88; H, 5.88.

(2S,4S)-1,2:4,5-Dianhydro-3-deoxypentitol ((S,S)-1). The spectroscopic data matched that obtained for the enantiomer: $[\alpha]^{24}_D$ = −55.5° (c = 0.92, $CHCl_3$). Anal. Calcd for $C_5H_8O_2$: C, 59.98; H, 8.05. Found: C, 59.84; H, 8.20.

(2R,4R)-1,5-Dibromo-2,4-pentanediol. (2R,4R)-1,5-Dichloro-2,4-pentanediol (2.28 g, 13.2 mmol, 1 equiv) was dissolved in 50 mL of ethyl ether and freshly powered KOH (5 g, 89 mmol, 6.7 equiv) was added in portions over 5 min. After being stirred for 30 min, the reaction mixture was filtered thru a plug of $MgSO_4$ and the ether was removed under reduced pressure from an ice bath. The resulting (2R,4R)-1,2:4,5-dianhydro-3-deoxypentitol was used directly in the next reaction.

A 0.4 M solution of Li_2NiBr_4 in THF[25] (100 mL, 40 mmol, 3.0 equiv) was added to the crude diepoxide. After stirring for 5 h at 25 °C, TLC analysis of the reaction mixture showed no more staring material. The mixture was diluted with saturated NH_4Cl solution, extracted (6 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure to give 3.36 g (12.5 mmol, 95%) of the product as white crystals. A small sample was recrystallized from CH_2Cl_2/hexanes: mp 95–97 °C; $[\alpha]^{25}_D$ = +29.3° (c = 0.765, CH_3OH); IR (KBr) 3350, 2964, 2896, 2874, 1437, 1417, 1389, 1321, 1275, 1162, 1093, 1043, 904, 658 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.11 (br s, 2 H), 3.53 (dd, J = 4.2, 10.4 Hz, 2 H), 3.42 (dd, J = 6.9, 10.3 Hz, 2 H), 2.66 (br s, 2 H), 1.80 (dd, J = 5.4, 6.6 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 68.2, 39.5, 39.2. Anal. Calcd for $C_5H_{10}Br_2O_2$: C, 22.93; H, 3.85; Br, 61.01. Found: C, 23.00; H, 3.83; Br, 60.93.

(4R,6R)-4,6-Bis(bromomethyl)-2,2-dimethyl-1,3-dioxane (9). A 3.36-g (12.5 mmol, 1 equiv) sample of (2R,4R)-1,5-dibromo-2,4-pentanediol was dissolved in a mixture of 40 mL of acetone and 20 mL of 2,2-dimethoxypropane with 30 mg of CSA. After 13 h the reaction was quenched with 2 mL of Et_3N and the volatiles were removed under reduced pressure. The crude

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product was purified by chromatography (SiO_2, 5% ethyl acetate/hexanes) to give 0.36 g (1.3 mmol, 11%) of recovered starting material and 3.12 g (10.3 mmol, 83%) of the product as a colorless oil: $[\alpha]^{25}_D$ = +19.1° (c = 1.52, CH_2Cl_2); IR (neat) 2987, 2959, 2857, 1438, 1419, 1380, 1246, 1220, 1197, 1157, 1131, 1043, 1016, 646 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.04 (m, 2 H), 3.38 (d, J = 5.8 Hz, 4 H), 1.83 (t, J = 7.7 Hz, 2 H), 1.40 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) *C* 101.3; *CH* 66.6; CH_2 35.4, 34.9; CH_3 24.6. Anal. Calcd for $C_8H_{14}Br_2O_2$: C, 31.82; H, 4.67. Found: C, 31.61; H, 4.88.

(6*S*,8*S*)-6,8-Tridecanediol. (2*R*,4*R*)-1,2:4,5-Dianhydro-3-deoxypentitol (154.0 mg, 1.54 mmol, 1 equiv) was dissolved in 15 mL of THF under argon, and the solution was cooled to −78 °C. To this were added 2.46 mL (6.16 mmol, 4 equiv) of 2.5 M butyllithium solution and 0.76 mL (6.16 mmol, 4 equiv) of BF_3·OEt_2. After stirring for 25 min, excess MeOH was added, and the reaction mixture was warmed to rt. The crude residue was concentrated three times with methanol under reduced pressure and purified by chromatography (SiO_2, 30% ethyl acetate/hexanes), yielding 282.0 mg (1.31 mmol, 85%) of product as a white crystalline solid.

Preparation Using Cuprate. (2*R*,4*R*)-1,2:4,5-Dianhydro-3-deoxypentitol (86.7 mg, 0.867 mmol, 1.0 equiv) was added via syringe to a solution of $Bu_2Cu(CN)Li_2$ (2.60 mmol, 3.0 equiv) in THF (3 mL) at −78 °C. The reaction mixture was slowly warmed to 0 °C over 3 h. The reaction was quenched with 10% NH_4OH/NH_4Cl solution, extracted (4 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 30% ethyl acetate/hexanes) gave 157.8 mg (0.73 mmol, 84%) of the product as white crystals: mp 80–82 °C; $[\alpha]^{26}_D$ = +2.8° (c = 0.25, $CHCl_3$); IR (KBr) 3316, 2956, 2928, 2872, 2857, 1466, 1422, 1407, 1377, 1328, 1265, 1143, 1125, 1066, 1031, 930, 904, 830, 738, 704, 663 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.90 (m, 2 H), 2.73 (br s, 2 H), 1.57 (t, J = 5.6 Hz, 2 H), 1.55–1.28 (m, 16 H), 0.87 (t, J = 6.3 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) *CH* 69.3; CH_2 42.2, 37.4, 31.8, 25.4, 22.5; CH_3 13.9; MS (EI) 145.1216 (M − C_5H_{11}), 127, 109, 101, 98, 83, 70, 69, 67, 57, 56, 55, 43, 41, 29. Anal. Calcd for $C_{13}H_{28}O_2$: C, 72.15; H, 13.05. Found: C, 72.05; H, 12.80.

(3*S*,5*S*)-3,5-Heptanediol. (2*R*,4*R*)-1,2:4,5-Dianhydro-3-deoxypentitol (112 mg, 1.12 mmol, 1.0 equiv) was dissolved in 10 mL of THF under argon, and the solution was cooled to −78 °C. To this were added 3.20 mL (4.48 mmol, 4.0 equiv) of 1.4 M methyllithium solution and 551 μL (4.48 mmol, 4.0 equiv) of BF_3·OEt_2. After stirring for 40 min, the reaction was quenched with saturated $NaHCO_3$ solution, and the reaction mixture was warmed to rt. The mixture was extracted (3 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 40% ethyl acetate/hexanes) gave 93 mg (0.70 mmol, 61%) of the product as white crystals.

Preparation Using Cuprate. (2*R*,4*R*)-1,2:4,5-Dianhydro-3-deoxypentitol (90.7 mg, 0.907 mmol, 1 equiv) was added via syringe to a solution of $Me_2Cu(CN)Li_2$ (2.68 mmol, 3.0 equiv) in THF (3 mL) at −78 °C. The reaction mixture was slowly warmed to 5 °C over 3 h. The reaction was quenched with 10% NH_4OH/saturated NH_4Cl solution, extracted (4 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 40% ethyl acetate/hexanes) gave 95.7 mg (0.725 mmol, 80%) of the product as white crystals: mp 52–54 °C; $[\alpha]^{25}_D$ = +20.6° (c = 1.12, $CHCl_3$); IR (KBr) 3322, 2964, 2937, 2878, 1459, 1377, 1258, 1206, 1147, 1115, 1045, 1008, 978, 944, 823, 670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.87–3.79 (m, 2 H), 2.80 (s, 2 H), 1.58 (t, J = 5.6 Hz, 2 H), 1.56–1.44 (m, 4 H), 0.92 (t, J = 7.4 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) *CH* 70.9; CH_2 41.5, 30.4; CH_3 10.2; MS (EI) 114.1401 (M − H_2O), 103, 85, 83, 67, 59, 57, 56, 55, 45, 43, 41. Anal. Calcd for $C_7H_{16}O_2$: C, 63.60; H, 12.20. Found: C, 63.49; H, 12.27.

(2*S*,4*S*)-1,5-Diphenyl-2,4-pentanediol. (2*R*,4*R*)-1,2:4,5-Dianhydro-3-deoxypentitol (79.5 mg, 0.795 mmol, 1 equiv) was dissolved in 8 mL of THF under argon, and the solution was cooled to −78 °C. To this solution were added 1.59 mL (3.18 mmol, 4 equiv) of 2.0 M phenyllithium solution and 391 μL (3.18 mmol, 4 equiv) of BF_3·OEt_2. After stirring for 25 min, excess MeOH was added, and the reaction mixture was warmed to rt. The crude residue was concentrated three times with methanol under reduced pressure and purified by chromatography (SiO_2, 30% ethyl acetate/hexanes) to afford 192.0 mg (0.75 mmol, 94%) of the product as a crystalline solid: mp 87–88 °C; $[\alpha]^{28}_D$ = −1.6° (c = 0.83, $CHCl_3$); IR (CH_2Cl_2) 3453, 3054, 3029, 3986, 2944, 1603, 1496, 1453, 1421, 1265, 1082, 896, 734, 704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32–7.17 (m, 10 H), 4.20 (m, 2 H), 2.77 (d, J = 6.7 Hz, 4 H), 2.29 (d, J = 3.6 Hz, 2 H), 1.71 (t, J = 5.7 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) *C* 138.4; *CH* 129.5, 128.8, 126.7, 70.3; CH_2 44.2, 41.6; MS (EI) 238.1378 (M − H_2O), 165, 147, 146, 129, 121, 103, 92, 91. Anal. Calcd for $C_{17}H_{20}O_2$: C, 79.64; H, 7.87. Found: C, 79.74; H, 7.83.

(2*R*,4*R*)-1,5-Diphenyl-2,4-pentanediol. (2*S*,4*S*)-1,2:4,5-Dianhydro-3-deoxypentitol (70 mg, 0.70 mmol, 1 equiv) was added via syringe to a solution of $Ph_2Cu(CN)Li$ (2.18 mmol, 3.1 equiv) in THF (3 mL) at −78 °C. The reaction mixture was slowly warmed to 0 °C over 4 h. The reaction was quenched with 10% NH_4OH/saturated NH_4Cl solution, extracted (4 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 30% ethyl acetate/hexanes) gave 172 mg (0.67 mmol, 96%) of the product as white crystals: mp 91–92 °C; $[\alpha]^{23}_D$ = +3.5° (c = 3.30, $CHCl_3$). The spectroscopic data matched that obtained for the enantiomer. Anal. Calcd for $C_{17}H_{20}O_2$: C, 79.64; H, 7.87. Found: C, 79.75; H, 7.86.

(4*S*,6*S*)-2,2,8,8-Tetramethyl-4,6-nonanediol. (2*R*,4*R*)-1,2:4,5-Dianhydro-3-deoxypentitol (42.5 mg, 0.425 mmol, 1.0 equiv) was dissolved in 4 mL of THF under argon, and the solution was cooled to −78 °C. To this solution were added 0.61 mL (1.10 mmol, 2.6 equiv) of 1.8 M *tert*-butyllithium solution and 209 μL (1.70 mmol, 4.0 equiv) of BF_3·OEt_2. After stirring for 25 min, excess MeOH was added, and the reaction mixture was warmed to rt. The crude residue was concentrated three times with MeOH under reduced pressure and purified by flash chromatography (SiO_2, 30% ethyl acetate/hexanes) to give 16.9 mg (0.078 mmol, 18% yield) of the product as white crystals: mp 115–119 °C; $[\alpha]^{24}_D$ = −8.2° (c = 0.53, $CHCl_3$); IR (KBr) 3337, 2950, 2905, 1466, 1399, 1364, 1244, 1170, 1097, 1060, 1017, 990, 933, 852, 637 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.11 (m, 2 H), 2.27 (s, 2 H), 1.56 (t, J = 5.8 Hz, 2 H), 1.47 (dd, J = 8.2, 14.5 Hz, 2 H), 1.33 (dd, J = 2.7, 14.5 Hz, 2 H), 0.96 (s, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) *C* 30.3; *CH* 67.2; CH_2 51.2, 46.7; CH_3 30.1; MS (EI) 145.1224 (M − C_5H_{11}), 109, 101, 99, 83, 57, 43, 41. Anal. Calcd for $C_{13}H_{28}O_2$: C, 72.17; H, 13.04. Found: C, 71.95; H, 12.94.

(3*S*,5*S*)-1,7-Diphenyl-3,5-heptanediol. (2*R*,4*R*)-1,2:4,5-Dianhydro-3-deoxypentitol (91 mg, 0.91 mmol) was dissolved in 10 mL of THF under N_2, and the solution was cooled to −78 °C. To this solution were added 11 mL of 0.23 M benzyllithium (2.53 mmol, 2.8 equiv) and 335 μL (2.72 mmol, 3.0 equiv) of BF_3·OEt_2. After stirring for 40 min, the reaction was quenched with 3 mL saturated $NaHCO_3$ solution, and the solution was warmed to rt. The reaction mixture was extracted (3 × CH_2Cl_2), dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 30% ethyl acetate/hexanes) gave 216 mg (0.76 mmol, 84%) of the product as white crystals: mp 91–93 °C; $[\alpha]^{26}_D$ = −8.1° (c = 1.78, $CHCl_3$); IR (KBr) 3330, 3084, 3027, 2940, 2907, 2844, 1603, 1496, 1454, 1401, 1313, 1155, 1108, 1082, 1052, 931, 764, 750, 732, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31–7.16 (m, 10 H), 4.03–3.94 (m, 2 H), 2.77 (ddd, J = 5.9, 9.7, 13.8 Hz, 2 H), 2.68 (ddd, J = 6.7, 9.4, 13.8 Hz, 2 H), 2.41 (d, J = 4.3 Hz, 2 H), 1.92–1.70 (m, 4 H), 1.67 (t, J = 5.2 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) *C* 141.8; *CH* 128.3, 128.3, 125.7, 68.6; CH_2 42.5, 39.0, 32.0; MS (EI) 266.1677 (M − H_2O), 248, 144, 134, 117, 105, 104, 92, 91. Anal. Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.45; H, 8.33.

(4*S*,6*S*)-1,8-Nonadiene-4,6-diol. A 104.1-mg sample of (2*R*,4*R*)-1,2:4,5-dianhydro-3-deoxypentitol (1.04 mmol, 1.0 equiv) was dissolved in 5.0 mL THF under N_2 with a crystal of 1,10-phenantroline indicator, and the solution was cooled to −78 °C. Vinyllithium (0.78 M, Et_2O) was added until a brown color presisted and then 5.4 mL more (4.21 mmol, 4.0 equiv). Next, 500 μL of BF_3·OEt_2 (4.06 mmol, 3.9 equiv) was added, and the solution was stirred at −78 °C for 40 min and then quenched with MeOH, follow by 5 mL of 15% NaOH and 2 mL of 30% H_2O_2, and warmed to rt. This mixture was stirred overnight, and the aqueous layer was extracted (4 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography (SiO_2, 30% ethyl acetate/hexanes) gave 142.1 mg (0.91 mmol, 88%) of product as a colorless oil: $[\alpha]^{26}_D$ = +28.0° (c = 0.98, $CHCl_3$); IR

(neat) 3355, 3076, 3002, 2977, 2936, 1832, 1641, 1434, 1327, 1220, 1133, 1050, 995, 914, 872, 830 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.86–5.73 (m, 2 H), 5.15–5.00 (m, 4 H), 4.1–3.9 (m, 2 H), 2.80 (s, 2 H), 2.22 (t, J = 6.5 Hz, 4 H), 1.61 (dd, J = 5.3, 6.2 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) *C*H 134.69, 68.09; CH_2 118.09, 42.01, 41.53; MS (EI) 115.0748 (M – C_3H_5), 97, 71, 67, 41. Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 68.89; H, 10.15.

(5*S*,7*S*)-1,10-Undecadiene-5,7-diol. A 1.3-mL sample of allyltributyltin (4.19 mmol, 4.0 equiv) was dissolved in 3.0 mL of ether under N_2, and the solution was cooled to 0 °C. A solution of butyllithium (1.6 mL, 4.11 mmol, 4.0 equiv) was added, and the reaction mixture was stirred at 0 °C for 5 min and then allowed to warm to rt for 1 h. The solution was recooled to −78 °C and 104.9 mg of (2*R*,4*R*)-1,2:4,5-dianhydro-3-deoxypentitol was added in 1.0 mL of ether via canula. Due to the limited solubility of allyllithium in this solution, an additional 10 mL of ether was added to the reaction mixture. Next, 500 μL of BF_3·OEt_2 (4.06 mmol, 3.9 equiv) was added, and the solution was stirred at −78 °C for 40 min and then quenched with MeOH, followed by 5 mL of 15% NaOH and 2 mL of 30% H_2O_2 and warmed to rt. This mixture was stirred overnight, and the aqueous layer was extracted (4 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography (SiO_2, 100% hexanes to 20% ethyl acetate/hexanes) gave 147.5 mg (0.80 mmol, 77%) of product as a white solid: mp 40.0–41.5 °C; $[\alpha]^{24}_D$ = +7.2° (c = 1.03, $CHCl_3$); IR (KBr) 3289, 3080, 2977, 2930, 1642, 1449, 1410, 1350, 1134, 1105, 1059, 992, 912, 882, 834, 764, 641 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.89–5.76 (m, 2 H), 5.07–4.95 (m, 4 H), 3.94 (br s, 2 H), 2.64 (br s, 2 H), 2.25–2.05 (m, 4 H), 1.69–1.47 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) *C*H 138.20, 68.75; CH_2 14.75, 42.22, 36.28, 29.99; MS (EI) 129.0920 (M – C_4H_7), 111, 93, 85, 67, 55, 41. Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.65; H, 10.82.

(2*S*,4*S*)-1,5-Dicyano-2,4-bis(trimethylsiloxy)pentane. (2*R*,4*R*)-1,2:4,5-Dianhydro-3-deoxypentitol (140 mg, 1.40 mmol, 1.0 equiv) and trimethylsilyl cyanide (0.56 mL, 4.2 mmol, 3.0 equiv) were placed in a flask equipped with a cold finger condenser. To this was added 3 mg of KCN/18-crown-6 complex.[15] After refluxing for 3 h, 5 mL of saturated $NaHCO_3$ solution was added to neutralize the excess trimethylsilyl cyanide. The reaction mixture was extracted (3 × ethyl acetate), dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 10% ethyl acetate/hexanes) gave 315 mg (1.05 mmol, 76%) of the product as a slightly golden oil: $[\alpha]^{26}_D$ = +51.9° (c = 0.790, $CHCl_3$); IR (neat) 2958, 2901, 2251, 1421, 1378, 1253, 1220, 1109, 1050, 1029, 995, 974, 909, 842, 753, 689; ^1H NMR (300 MHz, $CDCl_3$) δ 4.13–4.05 (m, 2 H), 2.58 (dd, J = 5.4, 16.8 Hz, 2 H), 2.49 (dd, J = 5.3, 16.8 Hz, 2 H), 1.79 (t, J = 5.9 Hz, 2 H), 0.18 (s, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) *C* 117.2; *C*H 65.6; CH_2 44.3, 26.9; CH_3 0.4; MS (EI) 283.1296 (M – CH_3), 225, 216, 170, 147, 142, 129, 101, 73. Anal. Calcd for $C_{13}H_{26}N_2O_2Si_2$: C, 52.30; H, 8.78. Found: C, 52.06; H, 8.80.

(2*R*,4*S*)-1,2-Epoxy-4-nonanol. (2*R*,4*R*)-1,2:4,5-Dianhydro-3-deoxypentitol (90.9 mg, 0.91 mmol, 1.0 equiv) was dissolved in 9 mL of THF under argon, and the solution was cooled to −78 °C. To this solution were added 0.43 mL (1.0 mmol, 1.1 equiv) of 2.28 M butyllithium solution and 168 μL (1.36 mmol, 1.5 equiv) of BF_3·OEt_2. After stirring for 10 min, the reaction was quenched with 1 mL of saturated $NaHCO_3$, and the solution was warmed to rt. The mixture was extracted (2 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography (SiO_2, 30% ethyl acetate/hexanes) gave 110 mg (0.70 mmol, 76%) of the product as a clear, colorless oil: $[\alpha]^{26}_D$ = +19.5° (c = 0.55, $CHCl_3$); IR (neat) 3417, 2931, 2859, 1467, 1412, 1378, 1324, 1258, 1133, 1036, 930, 843, 825, 727 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.75 (m, 1 H), 3.09 (m, 1 H), 2.77 (t, J = 4.5 Hz, 1 H), 2.55 (dd, J = 2.8, 4.8 Hz, 1 H), 2.48 (d, J = 4.2 Hz, 1 H), 1.74 (ddd, J = 4.1, 8.8, 14.4 Hz, 1 H), 1.53 (ddd, J = 3.4, 6.5, 14.4 Hz, 1 H), 1.42–1.16 (m, 8 H), 0.83 (t, J = 6.4 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$, DEPT) *C*H 69.3, 50.3; CH_2 47.0, 39.2, 37.6, 31.8, 25.2, 22.6; CH_3 14.0; MS (EI) 140.1206 (M – H_2O), 127, 113, 109, 101, 98, 87, 83, 55, 41. Anal. Calcd for $C_9H_{18}O_2$: C, 68.30; H, 11.47. Found: C, 68.18; H, 11.47.

(2*S*,4*R*)-4,5-Epoxy-1-phenyl-2-pentanol. (2*R*,4*R*)-1,2:4,5-Dianhydro-3-deoxypentitol (134.3 mg, 1.34 mmol, 1.0 equiv) was dissolved in 12 mL of THF under argon, and the solution was cooled to −78 °C. To this solution were added 0.74 mL (1.48 mmol, 1.1 equiv) of 2.0 M phenyllithium and 247 μL (2.0 mmol, 1.5 equiv) of BF_3·OEt_2. After stirring for 20 min, the reaction was quenched with 1 mL saturated $NaHCO_3$, and the solution was warmed to rt. The mixture was extracted (2 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography (SiO_2, 30% ethyl acetate/hexanes) gave 187.6 mg (1.05 mmol, 79%) of the product as a clear, colorless oil: $[\alpha]^{26}_D$ = +11.1° (c = 0.68, $CHCl_3$); IR (neat) 3422, 3059, 3027, 3001, 2918, 1602, 1496, 1454, 1412, 1310, 1259, 1118, 1080, 1031, 1001, 924, 853, 828, 792, 748, 701 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.33–7.17 (m, 5 H), 4.02 (m, 1 H), 3.13 (dddd, J = 2.8, 4.0, 4.2, 6.8 Hz, 1 H), 2.80 (dd, J = 5.0, 13.6 Hz, 1 H), 2.78 (dd, J = 4.2, 4.9 Hz, 1 H), 2.73 (dd, J = 7.9, 13.6 Hz, 1 H), 2.55 (dd, J = 2.8, 4.9 Hz, 1 H), 2.34 (d, J = 3.8 Hz, 1 H), 1.84 (ddd, J = 4.0, 9.0, 14.4 Hz, 1 H), 1.58 (ddd, J = 3.4, 6.8, 14.4 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$, DEPT) *C* 138.2; *C*H 129.6, 128.6, 126.6, 70.2, 50.2; CH_2 47.1, 44.2, 38.9; MS (EI) 160.0909 (M – H_2O), 147, 129, 121, 103, 92, 91, 87, 69, 65, 41. Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.12; H, 7.92. Found: C, 73.95; H, 8.01.

(3*S*,5*R*)-5,6-Epoxy-1-phenyl-3-hexanol. (2*R*,4*R*)-1,2:4,5-Dianhydro-3-deoxypentitol (464 mg, 4.64 mmol, 1.00 equiv) was dissolved in 40 mL of Et_2O under argon, and the solution was cooled to −78 °C. To this solution were added 16.0 mL (5.0 mmol, 1.1 equiv) of a 0.31 M benzyllithium solution and 628 μL (5.1 mmol, 1.1 equiv) of BF_3·OEt_2. After stirring for 25 min, the reaction was quenched with 5 mL of saturated $NaHCO_3$ solution, and the mixture was warmed to rt. The mixture was extracted (3 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure. Flash chromatography (SiO_2, 40% ethyl acetate/hexanes) gave 750 mg of a mixture of the desired (3*S*,5*R*)-5,6-epoxy-1-phenyl-3-hexanol and (3*S*,5*S*)-1,7-diphenyl-3,5-heptanediol in a 7:1 ratio, respectively. These could be separated by Kugelrohr distillation (134 °C, 1 Torr) to give 549 mg of the pure epoxide (2.85 mmol, 62% yield) as white crystals: mp 47–49 °C; $[\alpha]^{24}_D$ = +5.5° (c = 1.33, $CHCl_3$); IR (KBr) 3346, 3084, 3060, 3025, 3000, 2938, 2918, 2857, 1600, 1493, 1452, 1425, 1414, 1355, 1289, 1258, 1223, 1167, 1122, 1092, 1062, 1030, 1004, 928, 919, 862, 843, 752, 701, 614 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.12 (m, 5 H), 3.89–3.79 (m, 1 H), 3.14 (dddd, J = 2.8, 4.0, 4.1, 6.3 Hz, 1 H), 2.85–2.63 (m, 2 H), 2.81 (dd, J = 4.0, 4.8 Hz, 1 H), 2.60 (dd, J = 2.8, 4.8 Hz, 1 H), 2.12 (d, J = 4.4 Hz, 1 H), 1.87–1.78 (m, 2 H), 1.87 (ddd, J = 4.1, 8.8, 14.5 Hz, 1 H), 1.64 (ddd, J = 3.4, 6.3, 14.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) *C* 141.8; *C*H 128.4, 128.3, 125.8, 68.5, 50.1; CH_2 46.8, 39.1, 39.1, 31.8; MS (EI) 174.1045 (M – H_2O), 160, 156, 143, 135, 133, 128, 117, 104, 92, 91, 87, 41. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.03; H, 8.32.

(4*S*,6*R*)-4-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-6,7-epoxy-1-heptene. A 108.9-mg sample of (2*R*,4*R*)-1,2:4,5-dianhydro-3-deoxypentitol (1.08 mmol, 1.0 equiv) was dissolved in 5.0 mL of THF under N_2 with a crystal of 1,10-phenantroline indicator, and the solution was cooled to −78 °C. Vinyllithium (1.04 M, Et_2O) was added until a brown color presisted and then 1.25 mL more (1.30 mmol, 1.2 equiv). Next, 175 μL of BF_3·OEt_2 (1.42 mmol, 1.3 equiv) was added and the solution was stirred at −78 °C for 30 min and then quenched with MeOH, followed by saturated $NaHCO_3$. This mixture was stirred overnight, and the aqueous layer was saturated with NaCl, extracted (4 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure from an ice bath to give 145 mg of a yellow oil. The resulting crude oil was dissolved in 4.0 mL of CH_2Cl_2. To this solution were added 402.2 mg of DMAP (3.30 mmol, 3.1 equiv) and 327.9 mg of TBSCl (2.18 mmol, 2.0 equiv), and it was stirred for 19 h. The reaction was quenched with saturated $NaHCO_3$, 30 mL of Et_2O was added, and the organic layer was washed with 1 N $NaHSO_4$ and brine. The solution was dried ($MgSO_4$) and the solvent removed under reduced pressure. Chromatography (SiO_2, 3% *tert*-butyl methyl ether/hexanes) gave 146.0 mg (0.60 mmol, 56%) of product as a colorless oil: $[\alpha]^{24}_D$ = +39.6° (c = 1.11, $CHCl_3$); IR (neat) 2955, 2929, 2857, 1639, 1472, 1409, 1362, 1256, 1090, 1066, 1003, 913, 836, 808 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.87–5.71 (m, 1 H), 5.06–5.00 (m, 2 H), 3.98–3.92 (m, 1 H), 3.04–2.98 (m, 1 H), 2.78 (t, J = 4.5 Hz, 1 H), 2.47 (dd, J = 2.7, 5.1 Hz, 1 H), 2.26 (t, J = 6.5 Hz, 2 H), 1.69–1.50 (m, 2 H), 0.89 (s, 9 H), 0.07 (s, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$, DEPT) *C* 18.10; *C*H 134.53, 69.73, 49.86; CH_2 117.36, 47.79, 42.63, 47.79; CH_3 25.87, −4.34, −4.73; MS (EI)

201.1301 (M - C_3H_5), 185, 169, 155, 143, 129, 115, 101, 93, 75, 73; MS (CI, CH_4) 243.1781 (M + H). Anal. Calcd for $C_{13}H_{28}O_2Si$: C, 64.41; H, 10.81. Found: C, 64.67; H, 10.75.

(2*S*,4*S*)-1-Phenyl-2,4-nonanediol. (2*R*,4*S*)-1,2-Epoxy-4-nonanol (94.6 mg, 0.60 mmol, 1 equiv) was dissolved in 10 mL of THF under argon, and the solution was cooled to -78 °C. To this solution were added 0.60 mL (1.2 mmol, 2.0 equiv) of 2.0 M phenyllithium solution and 148 μL (1.20 mmol, 2.0 equiv) of BF_3·OEt_2. The reaction mixture was stirred for 20 min, quenched with excess MeOH, warmed to rt, and concentrated (3 × MeOH) under reduced pressure. Chromatography (SiO_2, 20% ethyl acetate/hexanes) gave 114.0 mg (0.48 mmol, 80%) of the product as a crystalline solid.

Preparation from (2*S*,4*R*)-4,5-Epoxy-1-phenyl-2-pentanol. (2*S*,4*R*)-4,5-Epoxy-1-phenyl-2-pentanol (122.0 mg, 0.685 mmol, 1.0 equiv) was dissolved in 8 mL of THF under argon, and the solution was cooled to -78 °C. To this solution were added 1.10 mL (2.73 mmol, 4.0 equiv) of 2.48 M butyllithium solution and 335 μL (2.73 mmol, 4.0 equiv) of BF_3·OEt_2. After stirring for 50 min, the reaction was quenched with 5 mL of saturated $NaHCO_3$ and warmed to rt. The reaction mixture was then extracted (4 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography gave 89.2 mg (0.378 mmol, 55%) of the product as a crystalline solid. In addition a nonpolar compound was isolated, which was believed to be a borate complex of the desired product. Stirring this with SiO_2 in MeOH for 2 d gave an additional 12.9 mg (0.055 mmol, 8%) of the desired product.

Preparation from (2*S*,4*R*)-4,5-Epoxy-1-phenyl-2-pentanol Using Cuprate. (2*S*,4*R*)-4,5-Epoxy-1-phenyl-2-pentanol (94.5 mg, 0.531 mmol, 1.0 equiv) was dissolved in 1.0 mL of THF and added to $Bu_2Cu(CN)Li_2$ (2.45 mmol, 4.6 equiv) in THF under argon at -78 °C. The reaction mixture was allowed towarm to 0 °C over 3 h. The reaction was then quenched with 10% NH_4OH/saturated NH_4Cl solution, extracted (4 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography gave 106.3 mg (0.442 mmol, 85%) of the product as a crystalline compound: mp 101–102 °C; $[\alpha]^{26}_D$ = -1.9° (*c* = 0.26, $CHCl_3$); IR (KBr) 3334, 3054, 2986, 2928, 1498, 1458, 1420, 1265, 1080, 896, 739, 704 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.35–7.18 (m, 5 H), 4.15 (m, 1 H), 3.94 (m, 1 H), 2.87–2.67 (m, 4 H), 1.63 (t, *J* = 5.8 Hz, 2 H), 1.49–1.28 (m, 8 H), 0.87 (t, *J* = 6.4 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$, DEPT) *C* 138.4; *C*H 129.4, 128.6, 126.5, 70.2, 69.3; CH_2 44.1, 42.0, 37.5, 31.9, 35.5, 22.7; CH_3 14.1; MS (EI) 218.1680 (M - H_2O), 195, 145, 109, 92. Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.23; H, 10.24. Found: C, 76.03; H, 10.30.

(3*S*,5*S*)-3,5-Decanediol. (2*R*,4*S*)-1,2-Epoxy-4-nonanol (69.2 mg, 0.438 mmol, 1 equiv) was dissolved in 1 mL of THF and added via cannula to a solution of $Me_2Cu(CN)Li_2$ (1.79 mmol, 4.1 equiv) in THF under argon at -78 °C. The reaction mixture was slowly warmed to 0 °C over 3 h and kept at this temperature for an additional 1 h. The reaction was quenched with 10% NH_4OH/saturated NH_4Cl solution, extracted (4 × EtO_2), dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 25% ethyl acetate/hexanes) gave 63.8 mg (0.371 mmol, 84%) of the product as a crystalline compound: mp 36–38 °C; $[\alpha]^{28}_D$ = +15.3° (*c* = 0.97); IR (KBr) 3300, 2928, 1461, 1350, 1123, 1048, 991, 918, 821, 754 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.89–3.77 (m, 2 H), 2.75 (s, 2 H), 1.60–1.19 (m, 12 H), 0.92 (t, *J* = 7.4 Hz, 3 H), 0.87 (t, *J* = 6.4 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$, DEPT) *C*H 70.8, 69.1; CH_2 41.9, 37.5, 31.9, 30.3, 25.5, 22.7; CH_3 14.1, 10.1; MS (EI) 156.1506 (M - H_2O), 127, 109, 103, 101, 98, 85, 83, 67, 59, 56, 55, 41, 29. Anal. Calcd for $C_{10}H_{22}O_2$: C, 68.92; H, 12.72. Found: C, 69.05; H, 12.69.

(5*S*,7*S*)-8-Phenyl-1-octene-5,7-diol. (2*S*,4*R*)-4,5-Epoxy-1-phenyl-2-pentanol (94.5 mg, 0.531 mmol, 1.0 equiv) was dissolved in 0.5 mL of THF and added to $(CH_2{=}CHCH_2)_2Cu(CN)Li$ (1.88 mmol, 3.5 equiv) in THF under argon at -78 °C. The reaction mixture was slowly warmed to 0 °C over 3 h. The reaction was then quenched with 3 mL of 10% NH_4OH/saturated NH_4Cl solution, extracted (4 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 30% ethyl acetate/hexanes) gave 94.2 mg (0.428 mmol, 81%) of the product as white crystals: mp 97.5–101 °C; $[\alpha]^{25}_D$ = -2.7 (*c* = 1.44, $CHCl_3$); IR (KBr) 3309, 3063, 3030, 2972, 2937, 2845, 1640, 1448, 1401, 1369, 1170, 1103, 1080, 1054, 1034, 906, 838, 753, 644, 601 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33–7.16 (m, 5 H), 5.81 (m, 1 H), 5.05–4.94 (m, 2 H), 4.15 (m, 1 H), 3.95 (m, 1 H), 2.77 (d, *J* = 6.6 Hz, 2 H), 2.60 (d, *J* = 4.8 Hz, 1 H), 2.45 (d, *J* = 3.7 Hz, 1 H), 2.20–2.03 (m, 2 H), 1.64 (t, *J* = 5.7 Hz, 2 H), 1.61–1.45 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) *C* 138.4; *C*H 138.5, 129.4, 128.7, 126.6, 70.2, 68.8; CH_2 114.9, 44.1, 42.0, 36.5, 30.2; MS (EI) 129.0874 (M - C_7H_7), 118, 117, 103, 93, 92, 85, 67, 55, 43, 41. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.50; H, 8.92.

(3*R*,5*R*)-1-Phenyl-3,5-decanediol. (3*R*,5*S*)-5,6-Epoxy-1-phenyl-3-hexanol (87 mg, 0.45 mmol, 1.0 equiv) was dissolved in 8 mL of THF under argon, and the solution was cooled to -78 °C. To this solution were added 0.73 mL (1.81 mmol, 4.0 equiv) of 2.48 M *n*-butyllithium solution and 222 μL (1.81 mmol, 4.0 equiv) of BF_3·OEt_2. After stirring for 30 min, the reaction was quenched with 5 mL of saturated $NaHCO_3$ solution, and the solution was warmed to rt. The reaction mixture was then extracted (3 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 20% ethyl acetate/hexanes) gave 90 mg (0.36 mmol, 80%) of the product as white crystals: mp 62–63.5 °C; $[\alpha]^{26}_D$ = +1.5° (*c* = 1.36, $CHCl_3$); IR (KBr) 3298, 3026, 2926, 2856, 1496, 1454, 1404, 1369, 1340, 1134, 1115, 1098, 1063, 1039, 933, 726, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30–7.15 (m, 5 H), 4.23–4.11 (m, 2 H), 3.22 (s, 1 H), 2.97 (s, 1 H), 2.78 (ddd, *J* = 5.8, 10.0, 13.7 Hz, 1 H), 2.67 (ddd, *J* = 6.6, 9.7, 13.7 Hz, 1 H), 1.88–1.73 (m, 2 H), 1.61 (t, *J* = 5.6 Hz, 2 H), 1.56–1.30 (m, 8 H), 0.90 (t, *J* = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) *C* 142.1; *C*H 128.4, 128.4, 125.9, 69.4, 68.8; CH_2 42.5, 39.1, 37.5, 32.3, 31.9, 25.5, 22.7; CH_3 14.1; MS (EI) 232.1828 (M - H_2O), 214, 161, 143, 134, 117, 104, 92, 91. Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 77.09; H, 10.25.

(2*R*,4*R*)-1-Cyano-6-phenyl-2,4-bis(trimethylsiloxy)hexane. (3*R*,5*S*)-5,6-Epoxy-1-phenyl-3-hexanol (306 mg, 1.59 mmol, 1.0 equiv) and 0.65 mL of trimethylsilyl cyanide (4.87 mmol, 3.1 equiv) were placed in a flask equipped with a cold finger condenser. To this was added 2 mg of KCN/18-crown-6 complex, and the reaction was heated to reflux.[15] After 3 h the reaction mixture was cooled to rt, and 5 mL of saturated $NaHCO_3$ solution was added to neutralize any excess trimethylsilyl cyanide. The reaction was extracted (3 × ethyl acetate), dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography gave 513 mg (1.41 mmol, 89%) of the product as a colorless liquid: $[\alpha]^{25}_D$ = -32.8° (*c* = 1.73, $CHCl_3$); IR (neat) 3086, 3063, 3028, 2955, 2250, 1603, 1496, 1454, 1416, 1378, 1252, 1107, 1033, 1002, 946, 842, 750, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32–7.11 (m, 5 H), 4.07 (m, 1 H), 3.86 (m, 1 H), 2.72–2.58 (m, 2 H), 2.58 (dd, *J* = 4.7, 16.7 Hz, 1 H), 2.46 (dd, *J* = 5.8, 16.7 Hz, 1 H), 1.85–1.69 (m, 4 H), 0.18 (s, 9 H), 0.14 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) *C* 141.9, 117.8; *C*H 128.4, 128.3, 125.9, 76.6, 69.1; CH_2 44.5, 39.7, 31.3, 27.2; CH_3 0.8, 0.4; MS (EI) 348.1789 (M - CH_3), 273, 258, 207, 183, 147, 142, 117, 91, 73. Anal. Calcd for $C_{19}H_{33}NO_2Si_2$: C, 62.76; H, 9.15. Found: C, 62.95; H, 8.92.

(4*S*,6*S*)-4-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1,9-decadien-6-ol. A 175-μL sample of allyltributyltin (0.56 mmol, 2.2 equiv) was dissolved in 2.0 mL of Et_2O under N_2, and the solution was cooled to 0 °C. Then 200 μL (0.51 mmol, 2.0 equiv) of 2.57 M butyllithium was added, and the solution was stirred at 0 °C for 5 min and then allowed to warm to rt for 1 h. The solution was recooled to -78 °C and 63.4 mg of [*S*-(*R**,*S**)]-(1,1-dimethylethyl)dimethyl[[1-(oxiranylmethyl)-3-butenyl]-oxy]silane was added in 1.0 mL of ether, via canula, and rinsed with an additional 1.0 mL of ether. Next, 60 μL of BF_3·OEt_2 (0.49 mmol, 1.9 equiv) was added and the reaction stirred for 40 min. MeOH was then added followed by 5.0 mL of 15% NaOH and 1.0 mL of 30% H_2O_2. This mixture was stirred vigorously for 3 h and then extracted (3 × Et_2O) and dried ($MgSO_4$), and the solvent was removed under reduced pressure. Chromatography (SiO_2, 5% *tert*-butyl methyl ether/hexanes) gave 61.1 mg (0.22 mmol, 85%) of product as a colorless oil: $[\alpha]^{24}_D$ = +13.2° (*c* = 1.14, $CHCl_3$); IR (neat) 3454, 3077, 2930, 2857, 1641, 1472, 1463, 1434, 1415, 1362, 1256, 1077, 1000, 912, 836, 808, 776, 736, 668 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.86–5.65 (m, 2 H), 5.08–4.92 (m, 4 H), 4.10–3.90 (m, 2 H), 3.21 (s, 1 H), 2.33 (t, *J* = 7.15 Hz, 2 H), 2.22–2.06 (m, 2 H), 1.58 (t, *J* = 5.0 Hz, 2 H), 1.60–1.40 (m, 2 H), 0.89 (s, 9 H), 0.084 (s, 3 H), 0.071 (s, 3 H); ^{13}C NMR (75

MHz, $CDCl_3$, DEPT) C 18.20; CH 138.85, 134.89, 71.40, 67.92; CH_2 117.63, 114.80, 41.59, 41.36, 37.30, 30.09; CH_3 26.06, -4.27, -4.59; MS (CI, CH_4) 285.2254 (M + H). Anal. Calcd for $C_{16}H_{32}O_2Si$: C, 67.55; H, 11.34. Found: C, 67.85; H, 11.23.

(3*R*,5*R*)-3-Benzoyl-5,6-epoxy-1-phenylhexanol (6). (3*S*,5*R*)-5,6-Epoxy-1-phenyl-3-hexanol (474 mg, 2.47 mmol, 1.0 equiv), benzoic acid (361 mg, 2.96 mmol, 1.2 equiv), and triphenylphosphine (766 mg, 2.96 mmol, 1.2 equiv) were dissolved in 10 mL of THF. The mixture was cooled to 0 °C and DEAD (466 μL, 2.96 mmol, 1.2 equiv) was added dropwise via syringe. After being stirred for 5 h, the reaction mixture was concentrated under reduced pressure. Flash chromatography (SiO_2, 10% ethyl acetate/hexanes) gave 631 mg (2.13 mmol, 86%) of the product as a colorless oil: $[\alpha]^{25}_D$ = +28.6° (*c* = 1.28, $CHCl_3$); IR (neat) 3060, 3027, 2997, 2923, 2861, 1715, 1601, 1584, 1496, 1452, 1359, 1314, 1274, 1176, 1112, 1070, 1026, 840, 750, 713, 701, 674 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.11–8.08 (m, 2 H), 7.58–7.16 (m, 8 H), 5.38 (m, 1 H), 3.08 (m, 1 H), 2.84–2.68 (m, 3 H), 2.48 (dd, *J* = 2.7, 5.0 Hz, 1 H), 2.28–1.88 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) C 166.0, 141.1, 130.2; CH 132.9, 129.5, 128.3, 128.3, 128.2, 125.9, 72.2, 48.9; CH_2 46.1, 37.1, 35.8, 31.7; MS (EI) 296.1421, 191, 174, 156, 143, 133, 130, 105, 91, 77. Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 77.19; H, 6.83.

(4*S*,6*R*)-8-Phenyl-1-octene-4,6-diol (7). (3*R*,5*R*)-3-Benzoyl-5,6-epoxy-1-phenylhexanol (96.2 mg, 0.325 mmol, 1.0 equiv) was dissolved in 10 mL of THF under argon, and the solution was cooled to -78 °C. To this solution were added 1.56 mL (1.62 mmol, 5 equiv) of 1.04 M vinyllithium solution and 200 μL (1.63 mmol, 5 equiv) of $BF_3{\cdot}OEt_2$. After stirring for 90 min, the reaction was quenched with 2 mL of MeOH, and the solution was warmed to rt. The reaction mixture was then treated with 3 mL of 15% NaOH solution and 1 mL of 30% H_2O_2 solution, and stirring was continued for 2 h. The reaction mixture was then extracted (3 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 30% ethyl acetate/hexanes) gave the product (50.3 mg, 0.229 mmol, 70%) as a colorless oil: $[\alpha]^{25}_D$ = +17.2° (*c* = 1.23, $CHCl_3$); IR (neat) 3355, 3063, 3026, 2938, 2861, 1642, 1603, 1496, 1454, 1326, 1093, 996, 916, 842, 748, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31–7.13 (m, 5 H), 5.79 (m, 1 H), 5.15–5.10 (m, 2 H), 3.93–3.84 (m, 2 H), 3.59 (br s, 1 H), 3.25 (br s, 1 H), 2.77 (ddd, *J* = 6.1, 9.5, 13.8 Hz, 1 H), 2.68 (ddd, *J* = 7.1, 9.1, 13.8 Hz, 1 H), 2.23 (m, 2 H), 1.88–1.47 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) C 141.8; CH 134.1, 128.3, 128.3, 125.7, 71.9, 71.8; CH_2 118.2, 42.5, 42.1, 39.5, 31.5; MS (EI) 202.1360 (M - H_2O), 184, 117, 104, 92, 91. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.17; H, 8.95.

(4*R*,6*R*)-6-(2-Phenylethyl)-3,4,5,6-tetrahydro-4-hydroxy-2*H*-pyran-2-one (8). (4*S*,6*R*)-8-Phenyl-1-octene-4,6-diol (74.8 mg, 0.340 mmol) was dissolved in 5 mL of CH_2Cl_2/MeOH (4:1). The solution was cooled to -78 °C and ozone was bubbled through until a blue color persisted. The solution was then degassed with air, followed by addition of 0.5 mL of dimethyl sulfide and warming to rt. After being stirred for 5 h, the reaction mixture was concentrated under reduced pressure. NMR of the crude residue showed it to be a 1:1 mixture of the anomeric methyl acetals. This crude mixture was dissolved in 0.05 M H_2SO_4 and stirred for 3 h at rt. This reaction mixture was then extracted (4 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure to give a mixture of the crude lactols. The crude lactols were dissolved in 5 mL of MeOH/H_2O (9:1), followed by addition of $NaHCO_3$ (1.15 g, 13.7 mmol) and bromine (175 μL, 3.4 mmol). After stirring for 4 h, the reaction was quenched with excess $Na_2S_2O_3$ solution, extracted (4 × Et_2O), dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography (Si_2O, 60% ethyl acetate/hexanes) gave 33.5 mg (0.152 mmol, 45% yield based on starting alkene) of the product[22] as a crystalline solid: mp 106–107 °C; $[\alpha]^{23}_D$ = +67.2° (*c* = 0.67, $CHCl_3$); IR (KBr) 3401, 3059, 3028, 2936, 2867, 1723, 1495, 1450, 1431, 1388, 1315, 1257, 1181, 1154, 1071, 1051, 755, 703, 601 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30–7.18 (m, 5 H), 4.70 (m, 1 H), 4.36 (m, 1 H), 2.87 (ddd, *J* = 5.5, 11.3, 13.7 Hz, 1 H), 2.78–2.69 (m, 2 H), 2.63 (ddd, *J* = 1.5, 3.6, 17.6 Hz, 1 H), 2.26 (br s, 1 H), 2.08–1.83 (m, 3 H), 1.75 (ddd, *J* = 3.2, 11.3, 14.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) C 170.7, 141.2; CH 128.7, 128.6, 126.3, 75.2, 62.9; CH_2 38.8, 37.5, 36.2, 31.3; MS (EI) 220.1112 (M^+), 202, 142, 129, 117, 104, 92, 91, 73, 43. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.87; H, 7.17.

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Nucleoside H-Phosphonates. 13. Studies on 3*H*-1,2-Benzodithiol-3-one Derivatives as Sulfurizing Reagents for H-Phosphonate and H-Phosphonothioate Diesters†

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Formation of O-oxidized products during sulfurization of H-phosphonothioate and H-phosphonate diesters with 3*H*-1,2-benzodithiol-3-one 1,1-dioxide (1) was found to be due to generation of the O-oxidizing agents, most likely 3*H*-2,1-benzoxathiol-3-one 1-oxide (4) and 3*H*-2,1-benzoxathiol-3-one (5), during the course of the reactions. Another source of the side products formation may be the disproportionation of 1 that occurs in the presence of triethylamine. To overcome these problems, a new sulfur-transferring reagent, 3*H*-1,2-benzodithiol-3-one (3), has been developed. Under aqueous reaction conditions, which are compatible with both solution- and solid-phase synthesis of oligonucleotides, the reagent 3 furnished clean and fast conversion of H-phosphonothioate and H-phosphonate diesters into the corresponding phosphoro*di*- and phosphoro*mono*thioates.

Introduction

Studies on nucleoside H-phosphonates as starting materials for oligonucleotide synthesis[1] have shown that this class of compounds also can be used for the preparation of various oligonucleotide analogues.[2] One most important class among such analogues constitutes oligonucleotides

† The H is being used to emphasize that the phosphonate is unsubstituted.

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