Highly Functionalized Cyclohexenyl Systems: Enzymatic Resolution and Selective Oxirane Opening Reactions of *p*-Benzoquinone Derivatives

Jeffrey T. Kohrt, Jian-Xin Gu, and Carl R. Johnson*

Department of Chemistry, Wayne State University, Detroit, Michigan 48202-3489

Received February 17, 1998

Diol **2**, derived in two steps from *p*-benzoquinone, was converted to epoxy alcohol **3**. The latter was resolved with crude *Candida rugosa* lipase in isopropenyl acetate/toluene to give acetate (−)-**4** and residual alcohol (+)-**3**. Oxirane ring opening reactions of **3** and the corresponding acetate and TBDMS derivatives with a variety of nucleophiles gave diastereomerically pure 3,4,5,6-tetrasubstituted cyclohexene derivatives of type **6**. X-ray crystal structures were obtained on compounds **6e**, **6m** and the diacetate prepared from **6l**. Nitrogen nucleophiles provided entry in various aziridines **10**. Pd(0)-catalyzed nucleophilic additions to substrate **5** cleanly provided the diastereomeric pattern of type **11**. *trans*-5,6-Disubstituted cyclohexadienes **13** were obtained by an unusual syn-reductive elimination on bromocarbonates **12** utilizing Pd or Zn.

Introduction

Our laboratory is engaged in a program that utilizes simple, achiral starting materials, such as cyclopentadiene, benzene, and cycloheptatriene, as starting materials for the synthesis of enantiopure, densely functionalized, bioactive targets.[1] Central to our strategy is the use of biocatalysis as a key step for the introduction of absolute stereochemistry.[2] Recently, we have initiated the use of *p*-benzoquinone as a starting material in an extension of our program's general methodology culminating in the synthesis of the bioactive epoxyquinol natural products (+)- and (−)-bromoxone, (+)- and (−)-harveynone, and (−)-tricholomenyn A.[3] Related to this project has been the formation of highly functionalized cyclohexenyl systems realized through regio- and stereoselective oxirane opening reactions of the *p*-benzoquinone-derived oxiranes **3**, **4** and **5**. Regio- and stereoselective vinyloxirane ring opening reactions have been well-studied and are involved as key steps in several synthetic schemes.[4] Indeed, the selective opening of the oxiranes in "*anti*-benzene dioxide" (*trans*-3,4,5,6-diepoxycyclohexene), derived from *p*-benzoquinone, has been investigated with various heteroatom nucleophiles resulting in C_2-symmetric products from bis-S_N2 addition. Alternatively, carbon nucleophiles have been shown to attack in a S_N2' fashion, often resulting in less predictable products.[5] In contrast to "*anti*-benzene dioxide", the reactivity of the monooxirane **3** remains little studied; this material is a potential source of unsymmetrical, heavily functionalized cyclohexenyl systems for further elaboration.[4d,5b,6]

Results and Discussion

Previously, we described the enzymatic resolution of a diacetate derivative of **2** formed by the bromination/reduction/acetylation of *p*-benzoquinone.[3a,7] While the resolution provided each enantiomer in high enantiomeric excess (ee), the yield of the (−)-diol was modest. In a related manner, the vinyloxirane **3**, which is readily available from *p*-benzoquinone in three steps, can be resolved effectively by *Candida rugosa* (*cylindracea*) lipase (CCL) (Scheme 1). Using 100% (w/w) crude CCL in toluene−isopropenyl acetate (IPA) (4:1) at room temperature for 36 h, the acetate (−)-**4** could be obtained with an ee of ≥98% in 45% yield while the recovered alcohol (+)-**3** could be isolated with an ee of 77% in 44% yield. Recrystallization of the enantiomerically enriched (+)-**3** from hexane/acetone raised the ee to ≥98%, as determined via chiral shift reagent analysis [300 MHz, (+)-Eu(hfc)$_3$] of the corresponding acetate (+)-**4**.[8]

In general, vinyloxiranes are known to be regioselectively opened by heteroatom nucleophiles at the allylic position.[4,5] In the course of our investigations with oxirane **5**, the lanthanide(III) Lewis acid, ytterbium triflate (Yb(OTf)$_3$), proved to be an efficient and mild catalyst for this transformation (Table 1).[9] Using Yb(OTf)$_3$ as a catalyst, oxirane **5** could be ring-opened at

(1) Johnson, C. R.; Adams, J. P.; Bis, S. J.; DeJong, R. L.; Golebiowski, A.; Medich, J. R.; Penning, T. D.; Senanayake, C. H.; Steensma, D. H.; Van Zandt, M. C. *Pure Appl. Chem.* **1992**, *64*, 1115.

(2) Enzymatic asymmetrization: Johnson, C. R.; Haridrishnan, L. S.; Golebiowski, A. *Tetrahedron Lett.* **1994**, *35*, 7735. Enzymatic resolution: Johnson, C. R.; Sakaguchi, H. *Synlett* **1992**, *35*, 6975.

(3) (a) Johnson, C. R.; Miller, M. W. *J. Org. Chem.* **1995**, *60*, 6674. (b) Johnson, C. R.; Miller, M. W. *J. Org. Chem.* **1997**, *62*, 1582.

(4) (a) Lindstrom, U. M.; Franckowiak, R.; Pinault, N.; Somfai, P. *Tetrahedron Lett.* **1997**, *38*, 2027. (b) Boaz, A. M. *Tetrahedron Asymmetry* **1995**, *6*, 15. (c) Ross, A. M.; Pohl, T. M.; Piazza, K.; Thomas, M.; Fox, B.; Whalen, D. L. *J. Am. Chem. Soc.* **1982**, *104*, 1658. (d) Taylor, R. J. K.; Haines, A. H.; Guo, Z.-X. *Synlett* **1993**, 607. (e) Hudlicky, T.; Luna, H.; Olivo, H. F.; Anderson, C.; Nugent, T.; Price, J. D. *J. Chem. Soc. Perkin Trans. 1* **1991**, 2907 (f) Balci, M.; Sutbeyaz, Y.; Secen, H. *Tetrahedron* **1990**, *46*, 3715. (f) Zipperer, B.; Hunkler, D.; Fritz, H.; Rihs, G.; Prinzbach, H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 309.

(5) (a) Tsuang, W.-S.; Griffin, G. W.; Horning, M. G.; Stillwell, W. G. *J. Org. Chem.* **1982**, *47*, 5339. (b) Esser, T.; Farkas, F.; Mangholz, S.; Sequin, U. *Tetrahedron*, **1994**, *50*, 3709. (c) Esser, T.; Sequin, U. *Tetrahedron Lett.* **1988**, *29*, 4405.

(6) Lehmann, J.; Moritz, A. *Carbohydr. Res.* **1993**, *239*, 317.

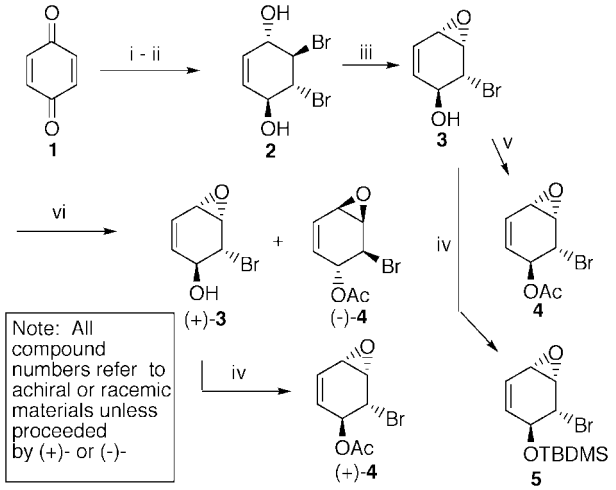
(7) Vogel, E.; Stegelmeier, H.; Altenbach, H. J. *Tetrahedron Lett.* **1978**, *36*, 3333.

(8) Koreeda, M.; Yoshihara, M. *J. Chem. Soc. Chem. Commun.* **1981**, 974.

(9) (a) Crotti, P.; Bussolo, V. D.; Favero, L.; Pineschi, M. *J. Org. Chem.* **1996**, *61*, 9548. (b) Crotti, P.; Bussolo, V. D.; Favero, L.; Pineschi, M. *Tetrahedron Lett.* **1994**, *35*, 6537. (c) Crotti, P.; Bussolo, V. D.; Favero, L.; Pineschi, M. *Tetrahedron Lett.* **1994**, *35*, 433. (d) Crotti, P.; Bussolo, V. D.; Favero, L.; Macchia, F.; Pineschi, M. *Tetrahedron Lett.* **1996**, *37*, 1675. (e) Ohno, H.; Mori, A.; Inoue, S. *Chem. Lett.* **1993**, 975.

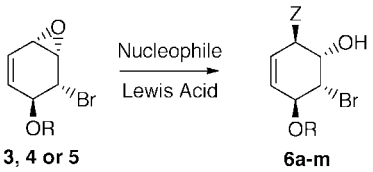
S0022-3263(98)00270-9 CCC: $15.00
Published on Web 06/27/1998

Scheme 1[a]



[a] Reagents and conditions: (i) Br_2, CH_2Cl_2; (ii) $NaBH_4$, 0 °C, H_2O-Et_2O, 62%; (iii) KOH, THF-MeOH, 90%; (iv) TBDMSOTf, Et_3N, CH_2Cl_2, 93%; (v) Ac_2O, CH_2Cl_2, Et_3N, 94%; (vi) CCL (100% w/w), toluene−IPA (4:1), 36 h ((+)-**3** 44%, (−)-**4** 45%).

Table 1. Lewis Acid-Assisted Oxirane Openings

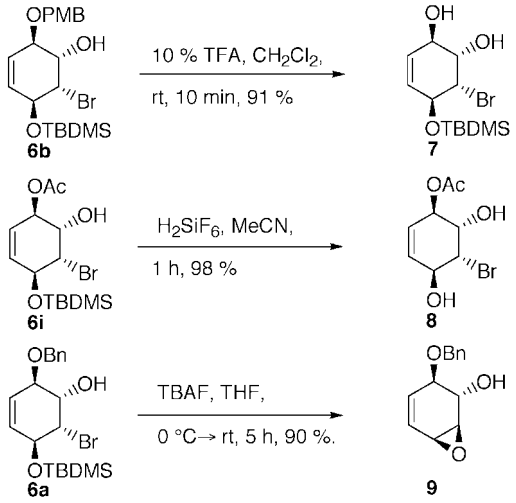


entry	starting material	R	conditions[a]	product	Z =	yield (%)
1	**5**	TBDMS	A	**6a**	BnO	87
2	**5**	TBDMS	A	**6b**	PMBO[b]	91
3	**5**	TBDMS	A	**6c**	BnNH	92
4	**5**	TBDMS	A	**6d**	TsNH	28[c]
5	**5**	TBDMS	A	**6e**	PMBNH[b]	78
6	**5**	TBDMS	B	**6f**	N_3	84
7	**5**	TBDMS	A	**6g**	PhS	80
8	**5**	TBDMS	C	**6h**	Br	86
9	**5**	TBDMS	D	**6i**	AcO	94
10	**3**	H	C	**6j**	Cl	94[d]
11	**3**	H	C	**6k**	Br	86[d]
12	**3**	H	C	**6l**	I	62[d]
13	**4**	Ac	D	**6m**	AcO	84

[a] A: CH_2Cl_2, $Yb(OTf)_3$ (0.3 equiv), ZH (3 equiv), 12−24 h. B: $ZnSO_4$, NaN_3, MeOH, 14 h. C: LiX, HOAc, THF, 12−24 h. D: (salen)Co(II) complex (see text) (0.1 equiv), Hunig's base, AcOH, *tert*-butyl methyl ether, O_2, 15 h. [b] PMB = 4-MeOBn. [c] Requires toluene reflux. [d] Isolated as diacetates.

the allylic position with alcohol, amine, and sulfur nucleophiles in high yields and with good regio- and stereoselectivies. Even the unreactive nucleophile *p*-toluenesulfonamide participates in the oxirane openings utilizing this catalyst. Other Lewis acids including $LiClO_4$[9c] and $BF_3{\cdot}OEt_2$[10] provided useful yields in some cases but did not prove to be general over a range of nucleophiles. The combination of zinc sulfate and sodium azide produced azido alcohol **6f** in high yields.[11] While oxirane openings with carboxylic acids are rare in the literature,[12] the new procedure developed by Jacobsen et al.[13a,b] incorporating a (salen)Co(II) complex (prepared from $Co(OAc)_2$ and (*S*,*S*)−(+)*N*,*N*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamine)[13c] efficiently facilitates oxirane opening of **5** with acetic acid to provide the differentially protected triol derivative **6i** in high yield. Oxirane **3** is subject to acetic acid-mediated nucleophilic attack by lithium halides to give regio- and stereoselective S_N2 ring openings (Table 1, entries 8,10−12).[14] In most cases (halides, azide, benzenethiol, and acetic acid), the S_N2 addition compound was the sole isolated product, while the ring-opening reactions with alcohol and amine nucleophiles resulted in 5% or less of diastereomeric byproducts which were not characterized. Proof of the regio- and stereochemistry was provided by X-ray crystal structures of various derivatives (**6e, 6m**, and the diacetate prepared from **6l**) or further elaboration to known compounds.

Scheme 2

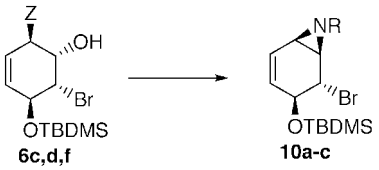


Interestingly, complex mixtures of products resulted from attempts to open **3** or **5** with water or hydroxide anion under a range of conditions. As an alternative, the diol **7** could be isolated efficiently after the removal of the *p*-methoxybenzyl protecting group of **6b** using 10% trifluoroacetic acid in dichloromethane.[15] Selective removal of the *tert*-butyldimethylsilyl protecting group in these systems can be accomplished under the conditions developed by DeShong (H_2SiF_6/MeCN),[16] as was exemplified for alcohol **8**. Alternatively, the use of tetrabutylammonium fluoride (TBAF) for the silyl group deprotection resulted in subsequent formation of another vinyloxirane system **9** which has the potential for further elaboration via another oxirane opening reaction (Scheme 2).

To verify the regio- and stereoselectivity of the products resulting from amine nucleophiles, vinylaziridines were prepared, as their formation relies on a 1,2-*trans*-amino alcohol arrangement.[11] These systems may prove to be of synthetic interest as many examples of aziridine ring-

(10) Hudlicky, T.; Tian, X.; Konigsberger, K.; Rouden, J. *J. Org. Chem.* **1994**, *59*, 4037.
(11) Muller, K.-H.; Kaiser, C.; Pillat, M.; Zipperer, B.; Froom, M.; Fritz, H.; Hunkler, D.; Prinzbach, H *Chem. Ber.* **1983**, *116*, 2492.
(12) (a) Posner, G. H.; *Angew. Chem., Intl. Ed. Engl.* **1978**, *17*, 487. (b) Nakajima, M.; Hasegawa, A.; Kurihara, N. *J. Liebigs. Ann.* **1965**, *689*, 235.
(13) (a) Jacobsen, E, N.; Kakiuchi, F.; Konsler, R. G.; Larrow, J. F.; Tokunaga, M. *Tetrahedron Lett.* **1997**, *38*, 773. (b) Martinez, L. E.; Leighton, J. L.; Carsten, D. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5897. (c) Leung, W.-H.; Chan, E. Y. Y.; Chow, E. K. F.; Williams, I. D. *J. Chem. Soc., Dalton, Trans.* **1996**, 1229.
(14) Bajaw, J. S.; Anderson, R. C. *Tetrahedron Lett.* **1991**, *32*, 3021.
(15) Kahre, D.; Yan, L. *Synlett* **1995**, 523.
(16) DeShong, P.; Pilcher, A. S. *J. Org. Chem.* **1993**, *58*, 5130.

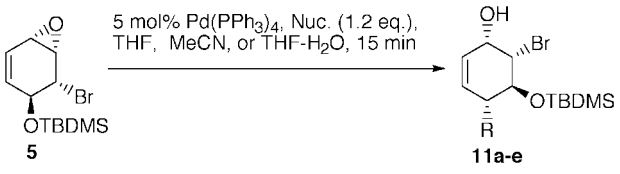
Table 2. Vinyl Aziridine Formation



entry	starting material	Z	conditions[a]	product	R	yield (%)
1	**6f**	N_3	A	**10a**	H	57
2	**6c**	BnNH	B	**10b**	Bn	52
3	**6d**	TsNH	C	**10c**	Ts	62

[a] A: Ph_3P, $PhCH_3$, 4 h; B: MeCN, CCl_4, Ph_3P, 14 h; C: i. Et_3N, MsCl, CH_2Cl_2; ii. MeOH, NaOMe.

Table 3. Pd(0)-Catalyzed Oxirane Openings

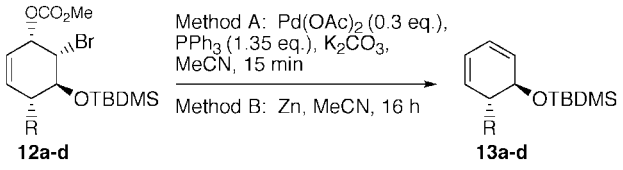


entry	nucleophile	product	R	yield (%)
1	$NaCH(CO_2Me)_2$	**11a**	$CH(CO_2Me)_2$	92
2	$CH_2(SO_2Ph)_2$	**11b**	$CH(SO_2Ph)_2$	83
3	$TsNH_2$/NaNHTs	**11c**	NHTs	67
4	$PhSO_2Na$	**11d**	SO_2Ph	48
5	NaN_3	**11e**	N_3	65

opening reactions have been recently published.[17] The choice of nitrogen nucleophile provided vinylaziridines with a wide range of *N*-substitution (Table 2). Treatment of azido alcohol **6f** with triphenylphosphine in refluxing toluene resulted in the formation of the unprotected aziridine **10a**.[18] Amino alcohol **6c** could be converted to the *N*-benzylaziridine **10b** with PPh_3/CCl_4 in MeCN.[19] A two-step approach was used for the formation of *N*-tosylaziridine **10c**; mesylation of **6d** followed by ring closure under basic conditions resulted in formation of **10c** in good yield.[20]

In addition to S_N2 ring openings, vinyloxiranes, in the presence of Pd(0)-catalysts, are known to form π-allyl palladium complexes which can be captured by various nucleophiles.[21] As a consequence of the stereospecific nature of both the formation of the π-allyl palladium complex and its reaction with carbanions, the Pd(0)-catalyzed oxirane ring openings of **5** occurred to provide single diastereomers in good yields (Table 3). It is known with vinyloxiranes, that such reactions can proceed without the addition of an external base, as the intermediate alkoxide behaves as an internal base toward the substrate.[21a] Although, in the present case of dimethyl malonate, addition of NaH was found to be advantageous. In contrast, when using bis(phenylsulfonyl)methane as a nucleophile, the reaction was sluggish when its corresponding carbanion was used but occurred smoothly under neutral conditions. For the formation of **11d** and **11e**, the sodium salts $PhSO_2Na$ and NaN_3 proved to be efficient nucleophiles when the reactions were conducted at 0 °C. TsNHNa gave poor results, but with a mixture of $TsNH_2$ and TsNHNa, the reaction took place rapidly under mild conditions.

Table 4. Diene Formation *via* syn-Elimination



entry	starting material	R	product	yield (%) method A	yield (%) method B
1	**12a**	$CH(CO_{2Me})_2$	**13a**	91	73
2	**12b**	$CH(SO_{2Ph})_2$	**13b**	88	71
3	**12c**	NHTs	**13c**	89	68
4	**12d**	SO_{2Ph}	**13d**		46

Further elaboration of the addition products **11** were realized after conversion of alcohols **11a**−**d** to their methyl carbonate derivatives **12a**−**d** under standard conditions (methyl chloroformate, pyridine, yields 90−93%). In a study of some Pd-catalyzed reactions of **12**, it was discovered that diene products were formed. Formation of the dienes was maximized by treatment of these carbonates with a catalytic amount of $Pd(OAc)_2$ in the presence of excess PPh_3 and K_2CO_3. These conditions resulted in a syn-elimination of the carbonate and bromo groups to furnish cyclohexadiene intermediates **13a**−**c** containing 5,6-trans substituents (Table 4). An effective molar ratio of 1:4.5 of $Pd(OAc)_2$:PPh_3 was determined to be crucial to this reaction. It is thought that these reactions occur by reduction of Pd(II) to Pd(0) by the phosphine, followed by formation of a π-allyl complex which is reduced by nucleophilic attack on the bromine substituent by additional phosphine. A number of examples of diene formation in the presence of Pd are known.[22] The same transformations were also effected by refluxing the carbonates in CH_3CN in the presence of activated Zn powder. The yields were slightly lower than in the Pd(II)-catalyzed system, probably due to the instability of this 1,4-conjugated diene upon prolonged heating.

In summary, oxiranes **3**−**5**, derived form *p*-benzoquinone, have been shown to participate in various regio- and stereoselective oxirane-opening reactions. Lewis acid catalysis provided products resulting from a direct nucleophilic ring opening, while Pd(0) catalysis furnished products stemming from an S_N2' addition. The resulting intermediates can be further elaborated into functionalized cyclohexenyl and cyclohexadienyl systems. The enzymatic resolution of **3** has been accomplished to provide the enantiopure derivatives (+)-**3** and (−)-**4**. These stereochemically defined intermediates should prove useful in the synthesis of various target molecules.

Experimental Section

***rel*-(1*R*,2*S*,3*R*,6*R*)-2-Bromo-7-oxabicyclo[4.1.0]hept-4-en-3-ol (3).** A solution of diol **2** (9 g, 33 mmol) in dry THF

(17) (a) Tanner, D. *Angnew. Chem. Intl. Ed. Engl.* **1994**, *33*, 599. (b) Kim, C. U.; Lew, W.; Williams, M. A.; Liu, H.; Ahang, L.; Swaminathan, S.; Bischofberger, N.; Chen, M. S.; Mendel, D. B.; Tai, C. Y.; Laver, W. G.; Stevens, R. C. *J. Am. Chem. Soc.* **1997**, *119*, 681. (c) Oguni, N.; Hoshimi, H.; Ono, K.; Hayashi, M *Tetrahedron Lett.* **1996**, *52*, 7817. (d) McCort, I.; Dureault, A.; Depezay, J.-C. *Tetrahedron Lett.* **1996**, *37*, 7717. (e) Hudlicky, T.; Olivo, H. F.; McKibben, B. *J. Am. Chem. Soc.* **1994**, *116*, 5108.

(18) Zamboni, R.; Rokach, J. *Tetrahedron Lett.* **1983**, *24*, 331.

(19) Kametani, T.; Kigawa, Y.; Ihara, M. *Tetrahedron* **1979**, *35*, 313.

(20) Hullar, T. L.; Baker, B. R. *J. Org. Chem.* **1965**, *30*, 4049.

(21) (a) Tsuji, J.; Kataoka, H.; Kobayashi, Y. *Tetrahedron Lett.* **1981**, *22*, 2575 (b) Larock, R. C.; Ding, S. *J. Org. Chem.* **1993**, *58*, 84.

(22) (a) Trost, B. M.; Fortunak, J. M. *J. Am. Chem. Soc.* **1980**, *102*, 2841. (b) Hauser, F. M.; Tommasi, R.; Hewawasam, P.; Rho, Y. S *J. Org. Chem.* **1988**, *53*, 4886.

(45 mL) at 0 °C was treated dropwise with powdered KOH (1.85 g, 33 mmol) in dry MeOH (20 mL) over 1.5 h. After the addition of KOH was completed, the mixture was stirred for 4 h at 0 °C and then diluted with EtOAc. Filtration, concentration, and purification by flash chromatography (3:1 hexanes:EtOAc) gave **3** (5.62 g, 89%) as a white solid: mp 81−82 °C (acetone/hexanes) (lit.[7] mp 79 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.90−2.92 (d, 1H, J = 4.8 Hz), 3.48−3.51 (dt, 1H, J = 2.4, 4.2 Hz), 3.73−3.74 (dd, 1H, J = 1.2, 4.2 Hz), 4.01−4.05 (dd, 1H, J = 1.2, 9.0 Hz), 4.44−4.48 (m, 1H), 5.88−5.92 (td, J = 1.8, 10.2 Hz, 1H), 6.01−6.06 (m, 1H); ^{13}C NMR (75 MHz, acetone-d_6) δ 51.4, 55.4, 56.1, 70.8, 123.3, 136.9.

(1*S*,2*R*,3*S*,6*S*)-2-Bromo-7-oxabicyclo[4.1.0]hept-4-en-3-ol [(+)-3], (1*R*,4*R*,5*S*,6*R*)-4-Acetoxy-5-bromo-7-oxabicyclo-[4.1.0]hept-2-ene [(−)-4], and (1*S*,4*S*,5*R*,6*S*)-4-Acetoxy-5-bromo-7-oxabicyclo[4.1.0]hept-2-ene [(+)-4]. A mixture of epoxide **3** (3.82 g, 20 mmol) and *Candida cylindrasea* lipase (3.82 g) in toluene/isopropenyl acetate (75 mL, 4:1) was stirred at room temperature for 36 h. Filtration, concentration, and purification by flash chromatography (hexane/EtOAc, 4:1) gave acetate (−)-**4** (2.14 g, 45%) as white crystals: mp 55−56 °C; $[\alpha]^{25}_D$ −182 (*c* 0.96, $CHCl_3$); ee ≥ 98% based on chiral shift reagent analysis; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.12 (s, 3H), 3.49−3.53 (dt, 1H, J = 1.8, 3.6 Hz), 3.74−3.76 (dd, 1H, J = 1.2, 3.6 Hz), 4.14−4.18 (dd, 1H, J = 1.2, 9.0 Hz), 5.55−5.60 (dt, 1H, J = 1.8, 9 Hz), 5.68−5.73 (dt, 1H, J = 1.8, 9.6 Hz), 6.08−6.13 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.83, 48.55, 51.15, 54.83, 72.73, 124.67, 132.33, 169.78.

Additionally, there was recovered 1.68 g (44%) of alcohol (+)-**3**: $[\alpha]^{25}_D$ +131 (*c* 1.03, $CHCl_3$) (optical purity ca. 75; after recrystallization from hexane/acetone: mp 114−115 °C; $[\alpha]^{25}_D$ 174 (*c* 1.0, $CHCl_3$); ee ≥ 98% [lit.[8] mp 101−102 °C; lit.[8] $[\alpha]^{25}_D$ +170.6 (*c* 0.812, $CHCl_3$)].

A sample of the pure alcohol (+)-**3** was converted to acetate (+)-**4** (see experimental for **4** below): mp 54 °C; $[\alpha]^{25}_D$ +182 (*c* 1.13, $CHCl_3$).

***rel*-(1*R*,4*R*,5*S*,6*R*)-4-Acetoxy-5-bromo-7-oxabicyclo[4.1.0]-hept-2-ene (4).** A solution of **3** (206 mg, 1.04 mmol) in CH_2Cl_2 (3.5 mL) at 0 °C was treated with Et_3N (217 μL, 1.56 mmol), acetic anhydride (118 μL, 1.26 mmol), and DMAP (1.3 mg, 0.104 mmol). The solution was allowed to warm to room temperature over 3 h and then concentrated under reduced pressure. The resulting oil was purified by flash chromatography (hexanes/EtOAc, 5:1) to reveal acetate **4** (207 mg, 85%) as a white solid: mp 83−85 °C (lit.[7] mp 78−78 °C); IR (film) 1743, 1370, 1226, 1046, 986, 871, 831 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.12 (s, 3H), 3.51 (ddd, 1H, J = 1.8, 4.0, 4.0 Hz), 3.75 (dd, 1H, J = 1.2, 3.6 Hz), 4.16 (dd, 1H, J = 1.2, 9.0 Hz), 5.57 (ddd, 1H, J = 2.4, 2.4, 9.0 Hz), 5.70 (ddd, 1H, J = 1.8, 1.8, 9.0 Hz), 6.10 (ddd, 1H, J = 3.6, 3.6, 9.0 Hz; ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.84, 48.56, 51.17, 54.83, 72.72, 124.67, 132.33, 169.79; MS (CI) *m*/*e* 233 $(M)^+$, 190 $(M - CH_3CO + H)^+$, 175 $(M - CH_3CO_2)^+$, 153 $(M - Br)^+$; HRMS (EI) calcd for $C_6H_7BrO_2$ $(M - CH_3CO + H)^+$ 189.9635, found 189.9629.

***rel*-(1*R*,4*R*,5*S*,6*R*)-5-Bromo-4-(*tert*-butyldimethylsilyl)-oxy-7-oxabicyclo[4.1.0]hept-2-ene (5).** A solution of **3** (1.3 g, 6.8 mmol) in CH_2Cl_2 (40 mL) at 0 °C was treated dropwise with Et_3N (808 mg, 8 mmol) and TBSOTf (1.98 g, 7.5 mmol). The solution was stirred at 0 °C for 1.5 h and then diluted with diethyl ether, washed with H_2O and brine, and dried over $MgSO_4$. Concentration of the organic solution and purification of the resulting oil by flash chromatography (hexane/EtOAc, 10:1) gave **5** (1.94 g, 93%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.1 (s, 3H), 0.16 (s, 3H), 0.91 (s, 9H), 3.45−3.48 (dt, 1H, J = 2.1, 3.9 Hz), 3.71−3.73 (dd, 1H, J = 1.2, 3.9 Hz), 3.98−4.01 (dd, 1H, J = 1.2, 8.4 Hz), 4.44−4.48 (td, 1H, J = 2.4, 8.4 Hz), 5.74−5.79 (td, 1H, J = 1.8, 9.6 Hz), 5.97−6.02 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.53, −4.46, 17.96, 25.74, 51.61, 54.08, 55.58, 72.02, 122.78, 137.10; HRMS (EI) calcd. for $C_{12}H_{21}BrO_2Si$ $(M)^+$ 304.0495, $(M - C_4H_9)^+$ 246.9790, found 246.9788.

***rel*-(1*R*,4*S*,5*S*,6*S*)-6-Bromo-5-(*tert*-butyldimethylsilyl)-oxy-2-benzyloxy-3-cyclohexen-1-ol (6a).** A solution of Yb(OTf)$_3$ (491 mg, 0.792 mmol), epoxide **5** (0.803 mg, 2.64 mmol), and benzyl alcohol (820 mL, 7.92 mmol) in CH_2Cl_2 (16 mL) was stirred at rt under N_2 for 24 h. H_2O (15 mL) was added to the mixture followed by extraction with diethyl ether (2 × 10 mL). The combined organic layers were washed with brine and dried over $MgSO_4$. Concentration under reduced pressure gave a yellow oil which was purified by flash chromatography (10:1 petroleum ether−EtOAc) to provide alcohol **6a** (890 mg, 82%) as a clear oil: IR (neat) 3442, 3034, 2953, 2928, 2856, 1496, 1471, 1389, 1253, 1097, 1057, 837, 777 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.10 (s, 3H), 0.12 (s, 3H), 0.89 (s, 9H), 2.44 (d, 1H, J = 4.8 Hz), 4.07−4.04 (m, 1H), 4.14−4.10 (m, 1H), 4.30 (dd, 1H, J = 2.8, 5.4 Hz), 4.48 (dd, 1H, J = 3, 5.1 Hz), 4.64 (d, 1H, J = 11.4 Hz), 4.69 (d, 1H, J = 11.4 Hz), 5.72 (dd, 1H, J = 3, 10 Hz), 5.83 (dd, 1H, J = 3, 10 Hz), 7.38 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.7, −4.5, 18.0, 25.7, 58.6, 70.5, 71.1, 71.9, 77.1, 126.5, 127.8, 127.9, 128.5, 129.0, 137.9; MS (CI) *m*/*e* 305 $(M - BnO)^+$, 281 $(M - TBSO)^+$, 249 $(M - BnO - t\text{-}Bu)^+$, 225, 201, 111, 91; HRMS (EI) calcd for $C_8H_{13}BrO_2Si$ $(M - BnO - t\text{-}Bu)^+$ 247.9868, found 247.9859.

***rel*-(1*R*,2*S*,5*R*,6*S*)-2-Acetoxy-6-bromo-5-(*tert*-butyldimethylsilyl)oxy-3-cyclohexen-1-ol (6i).** A mixture of (salen)Co(II) complex[13c] (Co(II) complex of (*S*,*S*)-(+)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamine) (13 mg, 0.021 mmol) and acetic acid (18 μL, 0.316 mmol) in *tert*-butyl methyl ether (TBME) (1 mL) was stirred under an oxygen atmosphere for 30 min. Epoxide **5** (50 mg, 0.214 mmol) in TBME (1 mL) was added followed by the addition of diisopropylethylamine (59 μL, 0.336 mmol). The mixture was stirred for 15 h under an oxygen atmosphere followed by the addition of 1 M citric acid (3 mL) and extraction with diethyl ether (2 × 2 mL). The combined diethyl ether layers were washed sequentially with 1 M $NaHCO_3$ and brine and then dried over $MgSO_4$. Concentration under reduced pressure and purification of the resulting black oil by column chromatography (3:1 petroleum ether/EtOAc) gave alcohol **6i** (72 mg, 94%) as a clear oil which solidified on standing to give white crystals: mp 66−67 °C (diethyl ether/pentane); IR (film) 3457, 2955, 2929, 2886, 2851, 1726, 1743, 1463, 1371, 1251, 1101, 1058, 837, 777 cm^{-1}; ^{1}H (300 MHz, $CDCl_3$) δ 0.10 (s, 3H), 0.12 (s, 3H), 0.89 (s, 9H), 2.11 (s, 3H), 2.61 (d, 1H, 7.0 Hz), 4.04−4.07 (m, 1H), 4.24 (ddd, 1H, J = 0.6, 2.6, 4.6 Hz), 4.51 (dd, 1H, J = 4.6, 4.6 Hz), 5.34−5.38 (m, 1H), 5.67 (ddd, 1H, J = 10, 2.6, 0.6 Hz), 5.78 (dddd, 1H, J = 10, 3.6, 1.3, 1.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.7, −4.6, 18.0, 21.0, 25.7, 58.1, 69.9, 70.8, 72.4, 125.4, 130.6, 171.0; MS (EI) *m*/*e* 307 $(M - C_4H_9)^+$, 249 $(M - C_4H_9 - OAc)^+$, 221, 167, 139, 117, 75, 43; HRMS (EI) calcd for $C_{10}H_{16}BrO_4Si$ $(M - C_4H_9)^+$ 307.0001, found 307.0006.

***rel*-(3*R*,4*S*,5*R*,6*S*)-3,5-Diacetoxy-4-bromo-6-chlorocyclohexene (Diacetate of 6j).** Glacial acetic acid (47 μL, 0.82 mmol) was added to a THF (2.5 mL) solution of LiCl (18.5 mg, 0.436 mmol) and epoxide **3** (52 mg, 0.27 mmol), and the reaction mixture was stirred for 12−24 h. H_2O (3 mL) was added to the mixture followed by extraction with diethyl ether (2 × 3 mL). The combined organic layers were washed with brine and dried over $MgSO_4$. Concentration of the organic solution gave the crude halo diol **6j**, which was then redissolved in CH_2Cl_2 (2 mL). Et_3N (114 μL, 0.816 mmol), Ac_2O (62 μL, 0.692 mmol), and DMAP (1 crystal) were added, and the solution was stirred for 3 h. Concentration of the reaction mixture and purification of the resulting oil by flash chromatography (5:1 petroleum ether/EtOAc) gave the diacetate of **6j** (80 mg, 94%) as an oil which solidified to white crystals on standing: mp 70−72 °C (diethyl ether/pentane); IR (film) 2945, 1744, 1430, 1372, 1224, 1049, 1013, 898, 800 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.11 (s, 3H), 2.14 (s, 3H), 4.48 (dd, 1H, J = 6.5, 3.0 Hz), 4.54−4.57 (m, 1H), 5.32 (dd, 1H, J = 5.7, 2.4 Hz), 5.60 (dd, 1H, J = 6.0, 3.0 Hz), 5.78 (dd, 1H, J = 10.5, 3.0 Hz), 5.93 (dd, 1H, J = 9.5, 3.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.7, 20.8, 46.7, 53.5, 71.0, 73.7, 126.2, 129.3, 169.7, 169.9; MS(EI) *m*/*e* 275 $(M - Cl)^+$, 173, 129, 111, 43; HRMS (EI) calcd for $C_{10}H_{12}BrO_4$ $(M - Cl)^+$ 274.9919, found 274.9919

***rel*-(1*R*,2*S*,5*S*,6*R*)-2-Acetoxy-6-bromo-3-cyclohexene-1,5-diol (8).** To a solution of alcohol **6i** (30 mg, 0.082 mmol) in MeCN (1 mL) in a plastic vial was added 1 drop of H_2SiF_6 (25% solution). The reaction was stirred for 4 h followed by the addition of 2 drops of saturated aqueous $NaHCO_3$ and

diethyl ether (3 mL). The solution was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the resulting oil by flash chromatography (1:1 petroleum ether/EtOAc) gave diol **8** (19 mg, 96%) as a clear oil: IR (neat) 3393, 3034, 2921, 2851, 1718, 1365, 1243, 1076, 1013, 949, 879, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.10 (s, 3H), 2.42 (broad s, 1H), 2.69 (broad s, 1H), 4.11 (m, 1H), 4.31 (dd, 1H, J = 2.6, 6.3 Hz), 4.58 (m, 1H), 5.33 (dd, 1H, J = 4.3, 4.3 Hz), 5.78 (dd, 1H, J = 3.0, 13.9 Hz), 5.96 (dd, 1H, J = 3.0, 10 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0, 58.5, 69.9, 70.9, 71.2, 125.3, 131.2, 184.5; MS (EI) *m/e* 190 $(M - HC_2O_2)^+$, 128, 111, 86, 43; HRMS (EI) calcd for $C_6H_7BrO_2$ $(M - HC_2O_2)^+$ 189.9629, found 189.9632.

***rel*-(1*R*,4*S*,5*S*,6*R*)-4-Benzyloxy-7-oxabicyclo[4.1.0]hept-2-en-5-ol (9).** To a 0 °C solution of alcohol **6a** (90 mg, 0.218 mmol) in THF (2 mL) was added TBAF (1.0 *M*, 436 μL, 0.436 mmol). The reaction mixture was allowed to warm to rt and was stirred a total of 4 h before being quenched with saturated aqueous NH_4Cl (4 mL). The aqueous solution was extracted with diethyl ether (2 × 4 mL), and the combined organic layers were washed with brine and dried over Na_2SO_4. Concentration of the organic solution and purification of the resulting oil by flash chromatography (3:1 hexanes/EtOAc) gave epoxide **9** (40 mg, 85%) as a clear oil: IR (neat) 3440, 3030, 2867, 1643, 1496, 1454, 1391, 1250, 1070, 994, 810, 787, 740, 692 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.30 (d, 1H, J = 7.0 Hz), 3.26 (dd, 1H, J = 5.0, 5.0 Hz), 3.47 (app d, 1H, J = 7.0 Hz), 4.0−4.03 (m, 1H), 4.07−4.10 (m, 1H), 4.58 (d, 1H, J = 20 Hz), 4.70 (d, 1H, J = 20 Hz), 5.95 (ddd, 1H, J = 2.0, 5.0, 10 Hz), 6.1 (ddd, 1H, J = 16.5, 4, 3 Hz), 7.34−7.40 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 46.4, 57.2, 69.8, 71.5, 126.6, 127.9, 128.5, 133.4, 137.9; MS (EI) *m/e* 218 $(M)^+$, 189, 127, 91; HRMS (EI) calcd for $C_{13}H_{14}O_3$: 218.0942, found 218.0945.

***rel*-(1*R*,4*S*,5*S*,6*R*)-5-Bromo-4-[(*tert*-butyldimethyl)silyl]-oxy-7-azabicyclo[4.1.0]hept-2-ene (10a).** To a solution of azido alcohol **6f** (60 mg, 0.172 mmol) in toluene (3.5 mL) was added PPh_3 (56 mg, 0.215 mmol). The reaction mixture was stirred at rt for 1 h followed by heating at reflux for 3 h. The reaction mixture was allowed to cool and was concentrated under reduced pressure. Purification of the resulting oil by flash chromatography (petroleum ether/EtOAc, 8:1) gave aziridine **10a** (30 mg, 57%) as an oily solid: IR (neat) 3312, 3037, 2954, 2929, 2857, 1597, 1466, 1388, 1361, 1254, 1091, 838, 777 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.06 (s, 3H), 0.11 (s, 3H), 0.86 (s, 9H), 2.49 (dd, 1H, J = 4.0, 4.0 Hz), 2.88 (dd, 1H, J = 2.3, 2.3 Hz), 4.39 (ddd, 1H, J = 2.0, 2.0, 6.0 Hz), 4.45 (m, 1H), 5.79 (dd, 1H, J = 6.0, 9.9 Hz), 6.39 (dd, 1H, J = 4.9, 9.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ −4.8, −4.5, 17.7, 25.6, 29.1, 39.0, 46.9, 68.4, 125.3, 132.1; MS (EI) *m/e* 304 $(M)^+$, 246 $(M - H - C_4H_9)^+$, 224 $(M - Br)^+$, 166, 92, 75; HRMS (EI) calcd for $C_{12}H_{22}BrNOSi$ $(M)^+$ 303.0654, found 303.0661.

***rel*-(1*R*,4*S*,5*S*,6*R*)-7-Benzyl-5-bromo-4(*tert*-butyldimethylsilyl)oxy-7-azabicyclo[4.1.0]hept-2-ene (10b).** A solution of CCl_4 (213 μL, 2.20 mmol) and PPh_3 (230 mg, 262 mmol) in MeCN (19 mL) was stirred at rt for 1 h. Amino alcohol **6c** (91 mg, 0.22 mmol) in MeCN (9 mL) was added via cannula followed by the addition of Et_3N (154 μL, 1.10 mmol). The solution was stirred at rt for 12 h and then at reflux for 2 h. Concentration of the solution onto Na_2SO_4 and purification via flash chromatography (petroleum ether/EtOAc, 20:1) gave aziridine **10b** (49 mg, 57%) as a clear oil: IR (neat) 3029, 2953, 2928, 2855, 1496, 1466, 1396, 1361, 1253, 1083, 836, 777, 733, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.10 (s, 3H), 0.14 (s, 3H), 0.91 (s, 9H), 2.09 (dd, 1H, J = 3.6, 6.0 Hz), 2.48 (dd, 1H, J = 1.9, 6.0 Hz), 3.23 (d, 1H, J = 14 Hz), 3.94 (d, 1H, J = 13.6 Hz), 4.13 (dd, 1H, J = 3.0, 5.6 Hz), 4.46 (dd, 1H, J = 4.9, 4.9 Hz), 5.73 (dd, 1H, J = 3.6, 9.9 Hz), 6.19 (ddd, 1H, J = 1.3, 4.0, 9.6 Hz), 7.25−7.39 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6, −4.4, 18.2, 25.9, 36.7, 47.1, 51.9, 63.3, 70.7, 124.5, 126.8, 127.6, 128.2, 127.9, 131.8, 138.6; MS (EI) *m/e* 396 $(M)^+$, 338 $(M - C_4H_9)^+$, 314 $(M - Br)^+$, 264, 183, 91; HRMS (EI) calcd for $C_{15}H_{19}BrNOSi$ 336.0419, found 336.0427.

***rel*-(1*R*,4*S*,5*S*,6*R*)-6-Bromo-4-[(*tert*-butyldimethyl)silyl]-oxy-7-(*p*-toluenesulfonylamino)-7-azabicyclo[4.1.0]hept-2-ene (10c).** A solution of alcohol **6d** (40 mg, 0.84 mmol) and Et_3N (17.5 μL, 0.126 mmol) in CH_2Cl_2 (1 mL) was cooled to 5 °C and methanesulfonyl chloride (7.0 μL, 0.093 mmol) was added. The reaction mixture was then allowed to warm to rt over 3 h, concentrated under reduced pressure onto Na_2SO_4, and filtered through a plug of silica gel (petroleum ether/EtOAc, 4:1). The resulting crude oil was dissolved in methanol (1 mL) and NaOMe (13 mg, 0.231 mmol) was added; the reaction mixture was stirred for 12 h. H_2O (2 mL) was added and the aqueous solution was extracted with diethyl ether (3 × 3 mL). The combined diethyl ether extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The resulting crude oil was purified by flash chromatography (petroleum ether/EtOAc, 20:1−10:1) to give aziridine **10c** (23 mg, 62%) as an amber oil: IR (neat) 3048, 2954, 2928, 2856, 1597, 1467, 1359, 1331, 1254, 1161, 1091, 965, 866, 837, 778 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.03 (s, 3H), 0.58 (s, 3H), 0.81 (s, 9H), 2.44 (s, 3H), 3.34 (dd, 1H, J = 3.6, 6.6 Hz), 3.63 (dddd, 1H, J = 2.0, 2.0, 2.0, 7.0 MHz), 4.01 (dd, 1H, J = 2.3, 4.6 Hz), 4.41 (dd, 1H, J = 4.3, 4.3 Hz), 5.86 (dd, 1H, J = 4.3, 9.6 Hz), 6.06 (dd, 1H, J = 5.0, 9.0 Hz), 7.32 (d, 2H, J = 7.9 Hz), 7.82 (d, 2H, J = 8.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.8, −4.4, 17.9, 21.6, 25.6, 35.7, 44.9, 46.9, 69.4, 76.5, 123.7, 127.8, 129.7, 134.0, 144.6; MS (CI) *m/e* 458 (M^+), 402 $(M - C_4H_9)^+$, 378 $(M - Br)^+$, 321, 287, 155, 115, 91; HRMS (EI) calcd for $C_{15}H_{19}BrNO_3SiS$ $(M - C_4H_9)^+$ 400.0038, found 400.0025.

General Procedure for the Synthesis of 11. Epoxide **5** (152.5 mg, 0.5 mmol) in THF (2 mL) was added over 15 min to a solution (THF, CH_3CN, or THF/H_2O, 5 mL) of $Pd(PPh_3)_4$ (5−15 mmol %) and nucleophile (0.6 mmol) under an Ar atmosphere. The reaction was monitored by TLC until completion. H_2O was added to the reaction mixture followed by extraction with EtOAc (2 × 5 mL). The combined organics were washed with brine and dried over $MgSO_4$. Concentration of the organic solution and purification of crude product by flash chromatography gave the alcohol **11**.

***rel*-(1*R*,4*S*,5*R*,6*S*)-Dimethyl 2-[5-bromo-6-(*tert*-butyldimethylsilyl)oxy-4-hydroxy-2-cyclohexenylmalonate (11a).** Epoxide **5** (152.5 mg, 0.5 mmol) in THF (2 mL) was added over 15 min to a THF solution (5 mL) of $Pd(PPh_3)_4$ (5 mol %) and freshly prepared dimethyl sodiomalonate (NaH, 60% suspension in oil, 24 mg, 0.6 mmol and dimethyl malonate, 80 mg, 0.6 mmol). The reaction was monitored by TLC until completion. H_2O was added to the reaction mixture followed by extraction with EtOAc (2 × 5 mL). The combined organics were washed with brine and dried over $MgSO_4$. Concentration of the organic solution and purification of crude product by flash chromatography (hexanes/EtOAc, 3:1) gave the alcohol **11a** (201 mg, 92%) as a clear oil: IR (film) 3510, 2954, 2856, 1754, 1737, 1258, 1067, 838 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.15 (s, 3H), 0.19 (s, 3H), 0.89 (s, 9H), 2.36 (d, 1H, J = 7.5 Hz), 2.88−2.91 (m, 1H), 3.73 (s, 3H), 3.77 (s, 3H), 3.99 (d, 1H, J = 6 Hz), 4.21−4.23 (m, 2H), 4.35−4.39 (m, 1H), 5.73−5.84 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.22, −3.60, 18.22, 25.99, 45.15, 52.51, 52.70, 60.40, 67.01, 70.39, 127.85, 128.14, 168.28, 168.81. HRMS (EI) calcd for $(M - C_4H_9)^+$ $C_{13}H_{20}NBrO_6Si$ 379.0213, found 379.0220.

General Procedure for the Synthesis of Carbonates 12. A solution of **11a**−**e** (1 equiv) and pyridine (6 equiv) in CH_2Cl_2 (0.1 M) was cooled to 0 °C and treated dropwise with methyl chloroformate (5 equiv). The reaction mixture was stirred at 0 °C for 3 h and then at rt for 3 h. The reaction mixture was then washed with 1 M HCl, H_2O, and brine, and the organic solution was dried over Na_2SO_4. Concentration of the organic solution under reduced pressure and purification of the resulting oil by flash chromatography (4:1 hexanes: EtOAc) gave **12a**−**e** in 90−93% yield.

***rel*-(1*R*,4*S*,5*R*,6*S*)-Dimethyl 2-[5-Bromo-6-(*tert*-butyldimethylsilyl)oxy(4-methoxycarbonyl)oxy-2-cyclohexenyl]-malonate (12a):** colorless oil, IR (film) 2930, 2857, 1752, 1441, 1266, 838 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.16 (s, 3H), 0.20 (s, 3H), 0.90 (s, 9H), 2.92−2.96 (m, 1H), 3.73 (s, 3H), 3.77 (s, 3H), 3.80 (s, 3H), 4.02 (d, 1H, J = 6.9 Hz), 4.19−4.23 (dd, 1H, J = 5.4, 7.8 Hz), 4.28−4.32 (dd, 1H, J = 3.9, 7.5 Hz), 5.37 (m, 1H), 5.75−5.81 (ddd, 1H, J = 2.4, 3.9, 10.5 Hz), 5.86−5.90 (dd, 1H, J = 2.4, 10.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.31,

−3.75, 18.18, 25.92, 44.76, 52.48, 52.58, 52.65, 52.73, 54.98, 70.42, 72.37, 124.07, 130.20, 155.01, 168.00, 168.69; HRMS (EI) calcd for $C_{19}H_{31}BrO_8Si$ $(M)^+$ 494.0972, $(M - C_4H_9)^+$ 437.0267, found 437.0261.

General Procedure for the Synthesis of Diene 13. Procedure A. A mixture of **12a**−**e** (0.1 mmol), $Pd(OAc)_2$ (6.8 mg, 0.3 equiv), PPh_3 (35.4 mg, 1.35 equiv), and K_2CO_3 (300 mg) in CH_3CN (4 mL) was stirred at rt under Ar for 2 min and then at reflux for 15 min. The mixture was cooled to rt and filtered. Concentration and purification of the resulting oil by flash chromatography (hexanes:EtOAc, 6:1) gave the product **13a**−**c**.

Procedure B. A mixture of **12a**−**d** (0.1 mmol) and activated Zn powder (1 g) in CH_3CN (4 mL) was heated at reflux overnight Filtration and concentration of the reaction mixture followed by purification of the crude oil by flash chromatography gave the diene **13a**−**d**.

***rel*-(5*R*,6*S*)-5-(*tert*-Butyldimethylsilyl)oxy-6-Bis(methoxycarbonyl)methyl-1,3-cyclohexadiene (13a):** colorless oil, yield 91% (73% by procedure B); IR (thin film) 2954, 2857, 1756, 1739, 1473, 1436, 1235, 1157, 838 777 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.06 (s, 3H), 0.07 (s, 3H), 0.89 (s, 9H), 3.11−3.18 (m, 1H), 3.60 (d, 1H, J = 5.7 Hz), 3.73 (s, 3H), 3.75 (s, 3H), 4.32−4.37 (ddd, 1H, J = 1.2, 3.6, 10.2 Hz), 5.72−5.76 (dd, 1H, J = 3.6, 10.5 Hz), 5.90−5.98 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.84, −4.18, 17.99, 25.77, 42.83, 51.48, 52.21, 52.52, 68.23, 123.91, 124.07, 127.05, 129.45, 168.53, 169.16; HRMS (EI) calcd for $C_{17}H_{28}O_5Si$ $(M)^+$ 340.1706, $(M - C_4H_9)^+$ 283.1002, found 283.1000.

Acknowledgment. We gratefully acknowledge support of the National Science Foundation (CHE-9801679). We thank Dr. Mary Jane Heeg for the X-ray crystal stucture determinations.

Supporting Information Available: Experimental data for compounds **6b**−**h**, diacetates of **6j**, **6k** and **6l**, compounds **6m**, **7**, **11b**−**e**, **12b**−**e**, and **13b**−**d,** crystallographic data and ORTEP diagrams for **6e, 6m** and the diacetate prepared from **6l**, and ^1H and ^{13}C NMR spectra of compounds **3** − **13** (91 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.

JO980270O