Exploring the Reactivity of Dioxacyclic Compounds as a Route to Polysubstituted Decalins and Fused Polycycles

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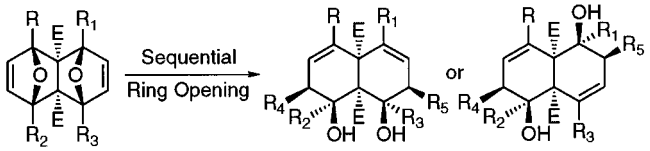
We have described a chemo-, regio-, and stereocontrolled methodology for the simple and efficient synthesis of a large variety of *cis*-decalins and related fused polycyclic systems with control at up to six stereocenters, based on the sequential ring-opening of dioxacyclic templates. We have established that the most useful feature of the reactivity of the dioxacyclic compounds toward the nucleophilic ring-opening reaction is that the first ring-opening reaction is significantly faster than the second allowing the sequential transformation of the oxabicyclic moieties. The flexibility of the sequential ring-opening process and its limitations have been demonstrated and a new enantioselective mode of opening was reported. The enantioselective base-induced desymmetrization was successfully applied to a thiadioxapentacycle to give the product in >95% ee using a chiral lithium amide base.

Introduction

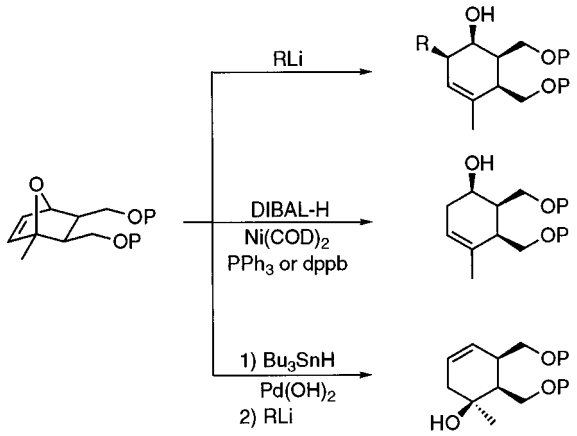
Oxygenated polycyclic systems are found in many natural products which exhibit wide-ranging biological activities. A leading challenge in organic synthesis is the development of new strategies which efficiently construct stereochemically rich and multifunctional polycyclic systems in a limited number of steps. We and others have used oxabicyclic templates and revealed their importance and value as intermediates, arising from their ability to be stereoselectivity ring-opened to highly functionalized cyclohexane derivatives.[1,2] Our objective was to design a strategy to rapidly prepare *cis*-decalins and related polycyclic compounds based on the sequential ring-opening of dioxacyclic templates (Scheme 1). We have recently reported the versatility of the "pincer" Diels−Alder reaction directed toward the rapid and facile construction of a variety of bridged polyheterocyclic ring systems[3] and demonstrated, in a preliminary report,[4] the use of the latter for the stereocontrolled synthesis of polysubstituted decalins and fused polycycles.

Various regio- and stereoselective ring-opening processes have been developed in our group over the past few years.[1] The most relevant to this study, namely, the nucleophilic ring-opening reaction,[1,5] the reductive nickel-catalyzed hydroalumination−fragmentation sequence,[6] and the palladium-catalyzed hydrostannation/tin−lithium exchange fragmentation sequence,[7] are shown in Scheme 2. In the nucleophilic ring-opening reaction, the stereochemistry is controlled by the exclusive attack on the *exo* face of the substrate.

Scheme 1



Scheme 2



In this report, we present the scope of the sequential ring-opening of a variety of dioxacyclic compounds for the stereoselective synthesis of highly functionalized *cis*-decalins and related fused polycyclic systems. Using the reactions described above, we have investigated the electrophilicity of the dioxacyclic dienes toward organolithium, and hydridic reagents via metal-catalyzed hydrometalation reactions. The issues of regio-, chemo-, enantio-, and stereocontrol in the sequential ring-opening reactions are addressed. A new based-induced ring-opening reaction will also be reported.

Results and Discussion

Substrate Preparation. The preparation of the required substrates commenced with the previously reported dioxacyclic dicarboxylic acid and diester systems[3] which were first reduced to the corresponding diols

[⊗] Abstract published in *Advance ACS Abstracts,* December 15, 1997.

(1) For recent reviews on the ring-opening of oxabicyclic systems, see: (a) Chiu, P.; Lautens, M. *Topics in Current Chemistry*; Springer-Verlag: Berlin, 1997, Vol. 190, p 1. (b) Woo, S.; Keay, B. *Synthesis* **1996**, 669. (c) Lautens, M. *Synlett* **1993**, 177. (d) For the recent use of dioxacyclic compound in synthesis: Mosimann, H.; Vogel, P.; Pinkerton, A. A.; Kirschbaum, K. *J. Org. Chem.* **1997**, *62*, 3002.

(2) For a recent review on aromatic heterocycles as intermediates in synthesis, see: Shipman, M. *Contemp. Org. Synth.* **1995**, *2*, 1.

(3) Lautens, M.; Fillion, E. *J. Org. Chem.* **1997**, *62*, 4418.

(4) Lautens, M.; Fillion, E. *J. Org. Chem.* **1996**, *61*, 7994.

(5) (a) For regioselective opening: Lautens, M.; Chiu, P. *Tetrahedron Lett.* **1993**, *34*, 773. (b) For intramolecular opening: Lautens, M.; Kumanovic, S. *J. Am. Chem. Soc.* **1995**, *117*, 1954.

(6) Lautens, M.; Ma, S.; Chiu, P. *J. Am. Chem. Soc.* **1997**, *119*, 6478.

(7) (a) Lautens, M.; Klute, W. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 442. (b) Lautens, M.; Aspiotis, R.; Colucci, J. *J. Am. Chem. Soc.* **1996**, *118*, 10930.

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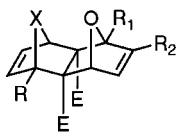
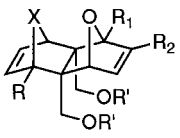
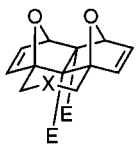
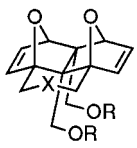
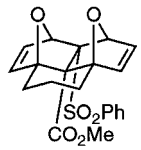
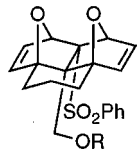
and further protected as the disilyl or dimethyl ethers (Tables 1 and 2).

Table 1. Dioxatetracyclic Substrate Preparation

Entry	Substrate			Product[a]		Yield[b], %
						
1	**1a**	X=O	R=R$_1$=R$_2$=H	E=CO$_2$H	**2a**	R'=H 34
2					**2b**	R'=TBDMS 89
3	**1b**	X=O	R=R$_1$=Me	E=CO$_2$H	**2c**	R'=H 72
4			R$_2$=H		**2d**	R'=TBDMS 98
5					**2e**	R'=Me 100
6	**1c**	X=NTs	R=R$_1$=Me	E=CO$_2$Me	**2f**	R'=H 80
7			R$_2$=H		**2g**	R'=TBDMS 90
8	**1d**	X=O	R=(CH$_2$)$_3$Cl	E=CO$_2$Me	**2h**	R'=H 59
9			R$_1$=Me R$_2$=H		**2i**	R'=TBDMS 91
10	**1e**	X=O	R=Me	E=CO$_2$Me	**2j**	R'=H 86
11			R$_1$=R$_2$=-(CH$_2$)$_4$-		**2k**	R'=TBDMS 74

[a] Reduction and protection, details in the Experimental Section. [b] Isolated yield of analytically pure product.

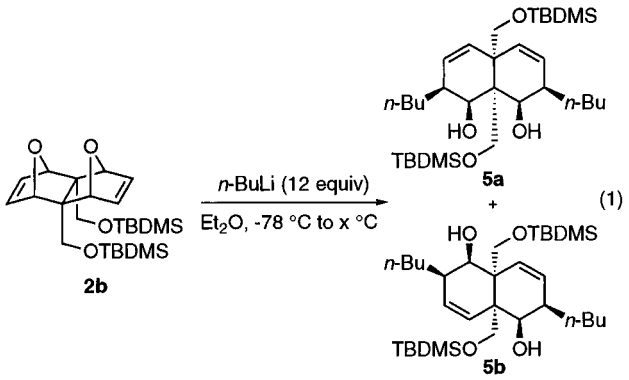
Table 2. Dioxapentacyclic Substrate Preparation

Entry	Substrate			Product[a]		Yield[b], %
						
1	**3a**	X=CH$_2$	E=CO$_2$Me	**4a**	R=H	87
2	**3b**	X=CH$_2$	E=CO$_2$H	**4a**	R=H	73
3				**4b**	R=TBDMS	74
4				**4c**	R=Me	97
5	**3c**	X=O	E=CO$_2$Me	**4d**	R=H	53
6				**4e**	R=TBDMS	85
7	**3d**	X=NBn	E=CO$_2$Me	**4f**	R=H	65
8				**4g**	R=TBDMS	85
9	**3e**	X=NPMB	E=CO$_2$Me	**4h**	R=H	88
10				**4i**	R=TBDMS	95
11	**3f**	X=NPMP	E=CO$_2$Me	**4j**	R=H	43
12				**4k**	R=TBDMS	93
13	**3g**	X=S	E=CO$_2$Me	**4l**	R=H	73
14				**4m**	R=TBDMS	91
						
15	**3h**			**4n**	R=H	85
16				**4o**	R=TBDMS	70

[a] Reduction and protection, details in the Experimental Section. [b] Isolated yield of analytically pure product.

Reduction of the dicarboxylic acid substrates **1a**, **1b**, and **3b** was performed in refluxing THF. The use of the milder reducing agent LiAlH(OMe)$_3$ was essential in these cases since LiAlH$_4$ gave ring-opened side products (triols) arising from the reductive ring cleavage of the oxabicyclic alkene moiety (~15% yield).[8] For the diester substrates, **1c**, **1e**, **3a**, **3c**−**g**, and the monoester **3h**, the reaction was performed at rt with LiAlH(OMe)$_3$ or LiAlH$_4$ without any side products. In the case of **1d**, the presence of a primary alkyl chloride group necessitated the use of a nonnucleophilic reducing agent like DIBAL-H giving the diol **2h** in 59% yield (Table 1, entry 8).

Unsubstituted Dioxatetracycle Nucleophilic Ring-Opening. We first explored the reactivity of the unsubstituted dioxatetracycle **2b** toward the nucleophilic ring-opening reaction. Treating **2b** with an excess of *n*-BuLi (12 equiv) at −78 °C to rt gave, after the sequential double ring-opening reactions, two regioisomeric *cis*-decalin diols **5a** and **5b** in a 2.8:1 ratio (eq 1).



(1)

In an attempt to improve the regioselectivity, a brief study of the effect of the temperature on the sequential nucleophilic ring-opening reactions was conducted (Table 3). Starting from −78 °C and further warming the solution to either −30 °C or 0 °C gave a mixture of regioisomeric decalins **5a** and **5b** with a preference for the meso decalin **5a** (Table 3, entries 2 and 3). The results showed that the temperature had little effect on the *regioselectivity* of the second ring-opening reaction. On the other hand, the *reactivity* of the second ring-opening was highly influenced by the temperature. At rt or 0 °C, the second ring-opening was complete after 8 h whereas at −30 °C, 48 h was necessary to obtain the bis-opened product **5a**. Lowering the temperature to −78 °C totally inhibited the opening of the remaining oxabicyclic moiety; the mono-opened product **5c** was isolated in 91% yield (Table 3, entry 4). In the optimization process, the number of equivalents of *n*-BuLi was reduced to 5 equiv giving **5c** after 5 h at −78 °C.

Table 3. Nucleophilic Ring-Opening of 2b, Temperature Effect

entry	temp, °C	time h,	ratio[a]	products[b]	yield,[c] %
1	rt	8	2.8/1	**5a**/**5b**	89
2	0	8	2.9/1	**5a**/**5b**	92
3	−30	48	3.3/1	**5a**/**5b**	77
4	−78	5	−	**5c**	91[d]

[a] Ratio measured by ^{1}H NMR. [b] Ring-opening, details in the Experimental Section. [c] Isolated yield of analytically pure products. [d] Five equivalents of *n*-BuLi were used.

The selective formation of the meso decalin **5a** was rationalized in terms of two distinct ring-opening reactions. The opening of the first oxabicyclic moiety generated a lithium alkoxide intermediate **5d** (M = Li). In the latter, the lithium alkoxide group and the butyl group

(8) Brown, H. C.; Weissman, P. M. *J. Am. Chem. Soc.* **1965**, *87*, 5614.

adopt a pseudoaxial and a pseudoequatorial orientation in a half-chair conformation. Because of the rigidity of the tricyclic system, the lithium atom may form a six-membered chelate with the remaining bridging oxygen (Figure 1). The lithium could then act as a Lewis acid assisting the C−O bond cleavage of the second ether bridge syn to the first alkoxide group in order to maintain the six-membered chelate. Attack at the anti position would give a seven-membered chelate which should not be as energetically favored. The tight chelation of the lithium alkoxide with the bridging ether may weaken one of the C−O bond and influence the electrophilicity of the two sp^2 carbons thus affecting the orientation of the S_N2' attack of the incoming nucleophile.[9]

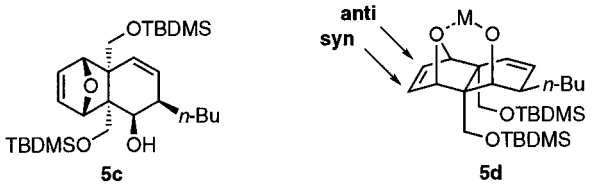
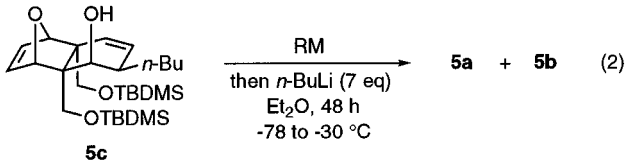


Figure 1.

We speculated that changing the counterion would enhance or even reverse the regioselectivity of the reaction (eq 2). Since the mono-opened "intermediate" **5c** could be isolated (Table 3, entry 4), the desired metal alkoxide intermediate **5d** could simply be generated via deprotonation with a basic organometallic reagent.



A loss in the selectivity was observed when the alcohol **5c** was deprotonated with BuMgBr prior to treatment with *n*-BuLi resulting in an equimolar mixture of decalins **5a** and **5b** (Table 4, entry 1). Deprotonation of **5c** with diethylzinc (Table 4, entry 2) gave similar results as the one-pot *n*-BuLi opening (Table 3, entry 3). Reacting **5c** with $(i\text{-Bu})_3Al$ to obtain the aluminum alkoxide intermediate gave a reversal in selectivity (Table 4, entry 3). This sequential double opening is complementary to the one-pot *n*-BuLi opening, and both decalins can be obtained selectively in good yields.

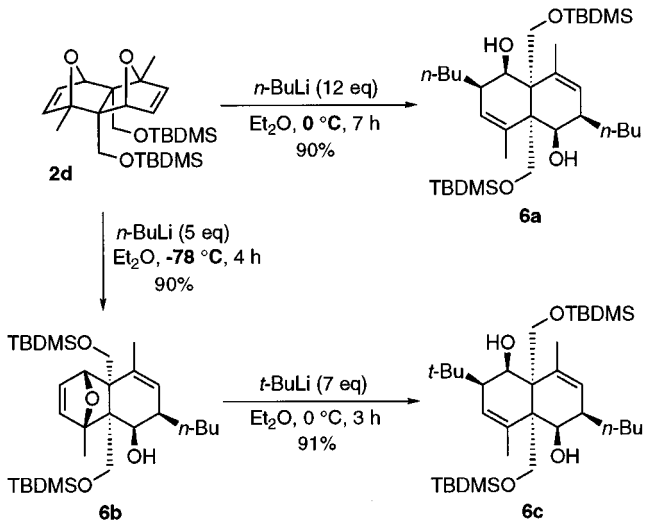
Table 4. Nucleophilic Ring-Opening of 5c

entry	RM	ratio[a,b] **5a**/**5b**	yield,[c] %
1	BuMgBr	1.2/1	79
2	Et_2Zn	2.7/1	80
3	$(i\text{-Bu})_3Al$	1/3.8	87

[a] Ratio measured by ^1H NMR. [b] Ring-opening, details in the Experimental Section. [c] Isolated yield of analytically pure product.

Substituted Dioxatetracycle Ring-Opening. The regioselective ring-opening reaction of a substituted dioxatetracycle was first studied with the "anti" dimethyl dioxatetracycle **2d** (Scheme 3). When **2d** was treated with excess *n*-BuLi at 0 °C for 7 h, the decalin **6a** bearing six stereocenters was obtained in 90% yield. The attack of

Scheme 3



the incoming nucleophile occurred exclusively at the position distal to the bridgehead substituents as observed previously for the simple oxabicyclic systems.[5a] The substituted system behaved like the unsubstituted dioxatetracyclic system **2b**, and the reactivity of the second oxabicyclic moiety was highly dependent on the temperature. Indeed, the mono ring-opening was easily achieved by simply performing the reaction at lower temperature. For example, treatment of **2d** at −78 °C for 4 h with 5 equiv of *n*-BuLi provided the mono ring-opened product **6b** in 90% yield. The subsequent reaction of **6b** with *t*-BuLi yielded the unsymmetrical decalin **6c**.

Surprisingly, MeLi, which usually fails to open bridgehead substituted oxabicyclo[2.2.1] systems, did induce the first opening on the dioxatetracycle **2e** after 24 h at rt (Table 5, entry 1).[10] Ring-opening under our reductive conditions was also examined. Attempted ring-opening on the free alcohol **7a** indicated the reaction was very sluggish and did not yield the expected product. To avoid the cleavage of the TBDMS ethers with DIBAL-H,[11] methyl ethers were used. Nickel-catalyzed reductive cleavage of **7b** provided the decalin **7c** in 78% yield (Table 5, entry 2).[6] The chemoselectivity of the hydroalumination is noteworthy since only the dioxacyclic olefin was hydroaluminated in the presence of a trisubstituted olefin. Finally, the hydrostannation−fragmentation sequence was applied to the dioxatetracycle **2d**. When **2d** was reacted with Bu_3SnH using Pearlman's catalyst[7b,12] or $Pd_2(dba)_3/PPh_3$,[7a] the bis(tributylstannyl) intermediate was obtained with high regioselectivity as judged by ^1H NMR. The latter was dissolved in THF and treated with an excess of *n*-BuLi (9 equiv) or MeLi (30 equiv) at 0 °C. The sequence of four reactions (bis-hydrostannation, bis-tin−lithium exchange, and ring-opening) generated the decalin **7d** bearing four contiguous quaternary stereocenters in 25% yield. The modest yield was attributable to the formation of several unidentified side products in the tin−lithium exchange step. The ^1H and ^{13}C NMR spectra of **7b** and **7d** were not resolved at rt and variable

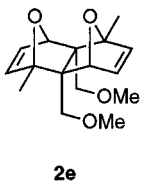
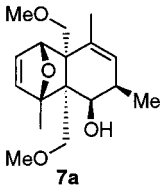
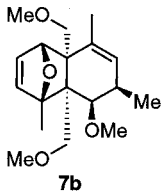
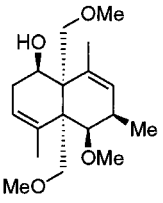
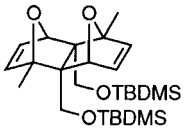
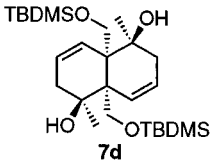
(9) Calvani, F.; Crotti, P.; Gardelli, C.; Pineschi, M. *Tetrahedron* **1994**, *50*, 12999.

(10) MeLi induces ring-opening of unsubstituted oxabicycles when TMEDA is used as the solvent. However, bridgehead-substituted substrates are inert toward MeLi, see: Lautens, M.; Belter, R. K. *Tetrahedron Lett.* **1992**, *33*, 2617.

(11) Corey, E. J.; Jones, G. B. *J. Org. Chem.* **1992**, *57*, 1028.

(12) Lautens, M.; Kumanovic, S.; Meyer, C. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1329.

Table 5. Dioxatetracycle Ring-Opening

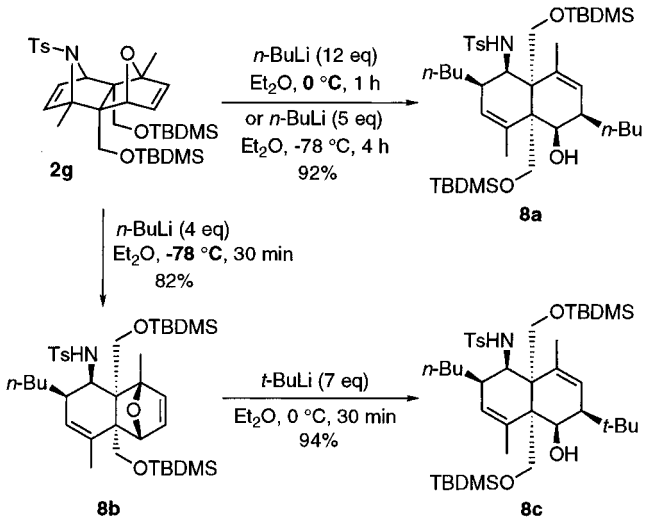
Entry	Substrate	Product[a]	Yield[b], %
1	 **2e**	 **7a**	40
2	 **7b**	 **7c**	78
3	 **2d**	 **7d**	25

[a]Ring Opening, details in the Experimental Section. [b]Isolated yield of analytically pure product.

temperature experiments were performed at 70−80 °C to obtain well resolved spectra.

Azaoxatetracycle and Unsymmetrical Dioxacycles Nucleophilic Ring-Opening. The reactivity of an azabicycle vs an oxabicycle in a nucleophilic ring-opening reaction was investigated using the azaoxatetracyclic substrate **2g**. Reaction of **2g** with an excess of *n*-BuLi at 0 °C produced the aminohydroxydecalin **8a** in 92% yield (Scheme 4). The addition was regioselective for both the aza and the oxa openings, occurring exclusively at the positions distal to the bridgehead substituents. This represents the first published example of a nucleophilic azabicyclic ring-opening.[13] Chemoselective ring-opening of the azabicyclic moiety over the oxabicyclic portion was observed when **2g** was reacted at lower

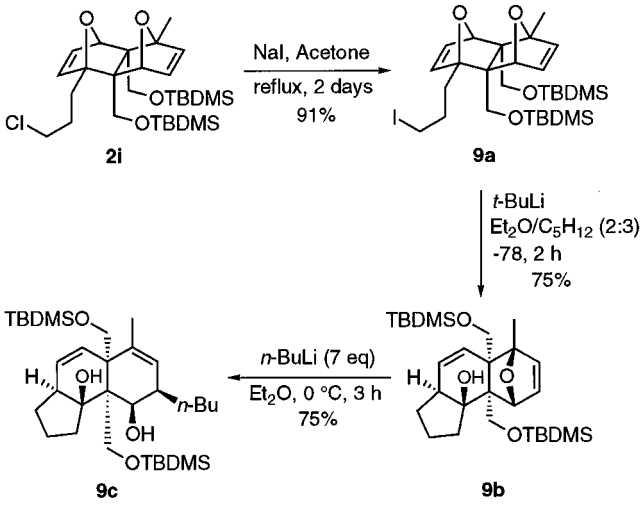
Scheme 4



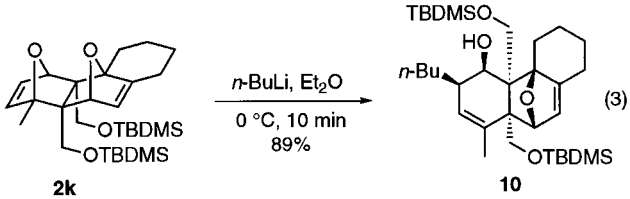
temperature with exactly 4 equiv of *n*-BuLi for a few minutes to give **8b** in 82% yield. Substrate **2g** was more reactive than the dioxatetracyclic substrate **2d**, and the reaction time as well as the number of equivalents of nucleophile were crucial in order to control the progress of the reaction. For example, reacting **2g** with only 5 equiv of *n*-BuLi at −78 °C gave exclusively the bis-opened product **8a** after 4 h. The chemoselectivity may be rationalized by comparing the pK_a's of the allylic leaving groups; 4-methylbenzenesulfonamide is a better leaving group than a secondary alcohol.[14] The subsequent reaction of **8b** with *t*-BuLi yielded the aminohydroxy decalin **8c** in excellent yield. The structure of **8c** was confirmed by X-ray crystallography.[15]

The sequential intramolecular−intermolecular nucleophilic ring-opening of the dioxacycle **2i** was also examined (Scheme 5). To carry out the halogen−lithium exchange, the alkyl chloride **2i** was transposed into the alkyl iodide **9a** under Finkelstein's conditions.[16] Treatment of **9a** with *t*-BuLi at −78 °C gave the alkyllithium intermediate which then cyclized giving **9b** in 75% yield.[5b] The attack of the internal nucleophile was assumed to occur exclusively on the *exo* face leading to a *trans* ring junction based on our earlier results.[5b] This is the first example of an intramolecular ring-opening of an oxabicyclic [2.2.1] system.[17] No trace of the *t*-BuLi ring-opening reaction was observed, although, a trace of the reduced product was detected. The ^{1}H and ^{13}C NMR spectra of **9b** were not well resolved at room temperature due to the presence of conformational isomers. The remaining oxabicyclic moiety in **9b** was opened with an excess of *n*-BuLi yielding the tricycle **9c** in 75% yield.

Scheme 5



A study of the reactivity of a disubstituted double bond *versus* a trisubstituted olefin toward nucleophilic ring-opening using **2k** was also investigated. Treatment of **2k** at 0 °C with an excess of *n*-BuLi gave exclusively the mono-opened product **10** (eq 3). The second oxabicyclic moiety resisted opening using *t*-BuLi at room temperature.[18]



Dioxapentacycle, Trioxapentacycle, and Azadioxapentacycle Ring-Opening. We also investigated the reactivity of dioxapentacyclic compounds in ring-opening reactions. A different reactivity profile was observed as is summarized in Table 6. Careful control of the reaction temperature led to the mono ring-opening of **4b** using *n*-BuLi, in excellent yield after 15 h at −78 °C (Table 6, entry 1). Enantioselective desymmetrization of **4b** using *n*-BuLi in the presence of (−)-sparteine in Et_2O gave **11a** in 56% ee.[19] MeLi also led to the mono ring-opening of **4c** after 24 h at rt although in modest yield (Table 6, entry 2). However, **4b** failed to undergo double opening

Table 6. Dioxapentacycle Ring-Opening

Entry	Substrate	Product[a]	Yield[b], %
1	**4b** R=TBDMS	**11a** R'=*n*-Bu	97
2	**4c** R=Me	**11b** R'=Me	41
3	**11a** R=TBDMS R'=*n*-Bu X=H	**11c** R"=*n*-Bu	78
4	**11a**	**11d** R"=*t*-Bu	84
5	**11e** R=Me R'=Me X=Me	**11f** R"=H	72
6	**11a**	**11g**	36

[a] Ring Opening, details in the Experimental Section. [b] Isolated yield of analytically pure product.

to **11c** regardless of the reaction temperature or the number of equivalents of *n*-BuLi leading instead to decomposition. To increase the reactivity of **11a** toward the second opening, a more Lewis acidic metal counterion

Table 7. Trioxapentacycle Ring-Opening

Entry	Substrate	Products[a]	Yield[b], %
1	**4e**	**12a** ratio = 1.6:1 **12b**	84
2	**12a**	**12c** ratio = 6.6:1 **12d**	70
3	**12b**	**12e** ratio = 10.1:1 **12f**	84

[a] Ring Opening, details in the Experimental Section. [b] Isolated yield of analytically pure product.

was added. Thus, **11a** was treated with 2 equiv of *n*-BuMgCl followed by 5 equiv of *n*-BuLi in the presence of THF to cleanly provide the bis-opened product **11c** (Table 6, entry 3). These conditions were also successful for the ring-opening of **11a** with *t*-BuLi to yield the tricycle **11d** (Table 6, entry 4). In this case, a combination *t*-BuMgCl/*t*-BuLi (2:5) was used since the transfer of the *n*-butyl group was observed when *n*-BuMgCl was used for the deprotonation step. We briefly investigated the reductive ring-opening of **11e** (Table 6, entry 5). As we had previously shown for **7a**, the dimethyl ether protected substrate was used and the free alcohol was protected as a methyl ether. Reductive ring-opening of **11e** via a nickel-catalyzed addition-β-elimination reaction provided the tricycle **11f** in 72% yield.[6] The structure of **11f** was confirmed by X-ray crystallography.[15] Finally, we investigated the reactivity of **11a** toward the hydrostannation−fragmentation sequence. No reaction occurred when **11a** was reacted with Bu_3SnH in the presence of $Pd_2(dba)_3/PPh_3$.[7a] However, using Pearlman's catalyst, a highly regioselective reaction was observed (95:5 by ^1H NMR).[7b,12] The hydrostannation of the oxabicyclic alkene was chemoselective toward the disubstituted double bond and protection of the free alcohol was unnecessary, in contrast to the hydroalumination reaction. After a quick purification to remove excess Bu_3SnH, further treatment of the crude organostannane product with a large excess of MeLi (18 equiv) gave the tricyclic diol **11g** in 36% yield. In this substrate, the tin−lithium exchange was sluggish and additional side products were detected.

The reactivity of the trioxapentacyclic **4e** was examined and shown to be significantly higher than the carbon analogue **4b**, giving a mixture of regioisomeric opened products **12a** and **12b** in a 1.6:1 ratio after few minutes at −78 °C in the presence of *n*-BuLi (Table 7, entry 1). This observation is in contrast to the opening of simple oxabicyclic [2.2.1] systems bearing an ether functionality

(13) We have preliminary evidence that azabicyclo[3.2.1] systems also react with organolithium reagent: Lautens, M.; Goldring, W.; Johnstone, S. Unpublished results.

(14) (a) Bordwell, F. G. *Acc. Chem. Res* **1988**, *21*, 456. (b) March, J. *Advanced Organic Chemistry* 4th ed.; Wiley-Interscience, Ed.; John Wiley & Sons: New York, 1992; p 248.

(15) The authors have deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

(16) Schröder, C.; Wolff, S.; Agosta, W. C. *J. Am. Chem. Soc.* **1987**, *109*, 5491.

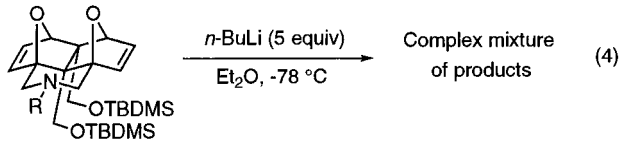
(17) The generality of this reaction is still under investigation: Lautens, M.; Fillion, E. Unpublished results.

(18) The reluctance of a trisubstituted double bond toward carbolithiation was previously reported in the literature: Krief, A.; Barbeaux, P. *Tetrahedron Lett.* **1991**, *32*, 417.

at the bridgehead position which were shown to undergo regioselective nucleophilic opening.[1b,c,20] The reasons for the loss in the regioselectivity and the high reactivity of this system are still unclear. Trioxapentacycle **4e** was very reactive yet also selective; the mono opening was achieved at −78 °C and no trace of bis-opened products was detected.

In contrast to the reaction of **4e**, **12a**, or **12b** underwent a regioselective ring-opening reaction. Treatment of **12a** with *t*-BuMgCl/*t*-BuLi (2:5) gave **12c** and **12d** in a 6.6:1 ratio (Table 7, entry 2). Alcohol **12b** reacted in a fashion similar to give a mixture of regioisomeric products **12e** and **12f** (10.1:1) in a combined yield of 84% (Table 7, entry 3).

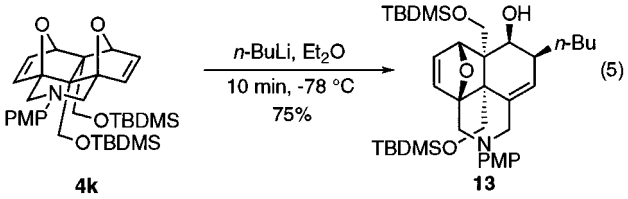
Unexpectedly, reacting the azadioxapentacyclic analogues **4g** and **4i** (PMB = *p*-methoxybenzyl) with 5 equiv of *n*-BuLi in Et_2O, gave after few minutes at −78 °C, a complex mixture of products in both cases (eq 4).



(4)

4g R = Bn
4i R = PMB

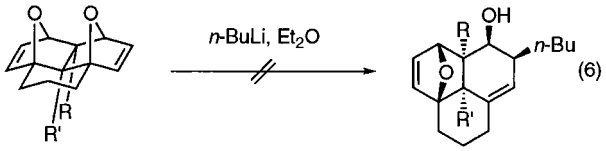
However, treatment of the parent *p*-methoxyphenyl (PMP) **4k** under the same conditions cleanly provided the mono-opened product **13** in good yield accompanied by three minor products which were not characterized (eq 5). The bis-opened product was obtained by treating **13** with the *t*-BuMgCl/*t*-BuLi (2:5) combination, and while the ^{1}H NMR of the crude reaction was very clean, all the efforts to purify and characterize the final tricycle were unsuccessful since the latter decomposed in less than 1 h at rt.



(5)

4k **13**

We have also showed that the presence of a phenyl sulfone in close proximity to the alkenes of the dioxacycles inhibited the nucleophilic ring-opening reaction of the dioxapentacycles **4o** and **14** (eq 6).

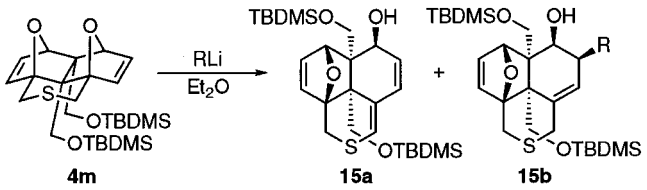


(6)

4o R = SO_2Ph R' = $CH_2OTBDMS$
14 R = H R' = SO_2Tol

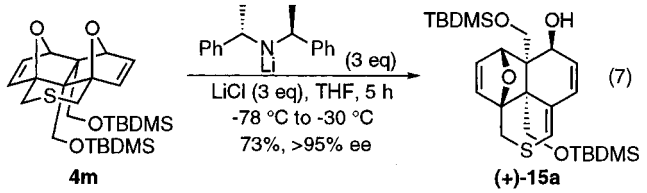
Enantioselective Desymmetrization. Thiadioxapentacycle and Azadioxapentacycle Base-Induced Ring-Opening. To have access to the "syn" dimethyl dioxatetracycle that would be complementary to the "anti" dimethyl substrate **2d**, the desulfurization of **4m** was envisaged. Unfortunately, all attempts to desulfurize were unsuccessful and gave, in most cases, the fully hydrogenated product without removal of the sulfur atom due to the high reactivity of the strained olefins. Nevertheless, a ring-opening study of the thiadioxapentacycle **4m** was undertaken since reduction was also possible following ring-opening. The reaction of **4m** with 5 equiv of *n*-BuLi at −78 °C was complete after 30 min and unexpectedly gave two products, **15a** and **15b**, in an equimolar ratio (Scheme 6). The alcohol **15b** was identified as the expected ring-opened product. The second product arose from the deprotonation of the methylene hydrogen adjacent to the sulfur atom, followed by fragmentation to give the thioether **15a**. This constitutes to our knowledge a novel mode of ring-opening which we have explored in some detail.[1a,21] Treating **4m** with the "less" nucleophilic MeLi gave exclusively **15a** in 82% yield after 18 h at rt.

Scheme 6



n-BuLi (5 equiv), 30 min, -78 °C	54	:	46	85%
MeLi (5 equiv), 18 h, rt	100	:	0	82%

We took advantage of this unexpected result and studied the base-induced ring-opening of **4m** in the presence of a chiral base.[22] The enantioselective desymmetrization of **4m** was achieved using 3 equiv of a lithium amide−LiCl complex (1:1) in THF generated from the hydrochloride salt of (−)-bis[(*S*)-1-phenylethyl]amine.[23] The tetracycle (+)-**15a** was obtained in >95% ee.[19a,b,24,25] The control of the temperature and the reaction time were critical in order to obtain a good yield of **15**, since longer reaction times gave a large amount of the *meso* bis-opened product. The absolute stereochemistry of (+)-**15a** has yet to be determined.



(7)

4m **(+)-15a**

We also examined the base-induced ring-opening of azadioxapentacycle. To be able to achieve the deproto-

(19) (a) The ee was determined using $Yb(hfc)_3$. (b) The sense of induction was not determined. (c) For the opening of *meso* oxabicyclo-[3.2.1] with *n*-BuLi/(−)-sparteine: Lautens, M.; Gajda, C.; Chiu, P. *J. Chem. Soc., Chem. Commun.* **1993**, 1193. (d) Gajda, C. M. Sc. Thesis, Ring-Opening Reactions of Oxabicyclic Compounds: Asymmetric Induction and Solvent Effects, University of Toronto, 1993.

(20) Chiu, P. Ph.D. Thesis, Ring-Opening Reactions of Oxabicyclic Compounds: Unsymmetrical Substrates and Reduction, University of Toronto, 1994.

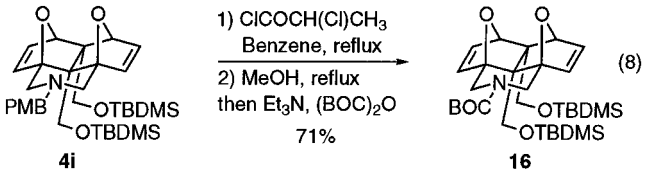
(21) For reported deprotonation/fragmentation of "unactivated" oxabicyclic compounds: (a) Arjona, O.; Conde, S.; Plumet, J.; Viso, A. *Tetrahedron Lett.* **1995**, *36*, 6157. (b) Lautens, M.; Ma, S. *Tetrahedron Lett.* **1996**, *37*, 1727.

(22) For a review on the synthesis of chiral compounds by bond disconnection, see: Gais, H.-J. In *Methods of Organic Chemistry* (Houben-Weyl), 1996; Vol. E 21a, Part C, p 589. (d) Ho, T. L. *Symmetry. A basis for synthetic design*; Wiley-Interscience, Ed.; John Wiley & Sons: New York, 1995.

(23) Majewski, M.; Lazny, R. *J. Org. Chem.* **1995**, *60*, 5825.

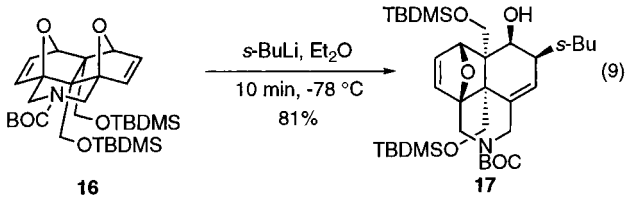
(24) For the synthesis of a symmetrical dioxapentacycle and its enantioselective desymmetrization by enantioselective hydroboration, see: Marchionni, C.; Vogel, P.; Roversi, P. *Tetrahedron Lett.* **1996**, *37*, 4149.

nation at the methylene position next to the nitrogen atom, the PMB (*p*-methoxybenzyl) protected amino substrate **4i** was transposed into the BOC protected amine **16** using the ACE-Cl (1-chloroethyl chloroformate) method in 71% yield (eq 8).[26]



4i **16**

Treatment of the BOC protected analogue **16** with *s*-BuLi in Et_2O at −78 °C did not give the desired base-induced ring-opened product, but instead, led to the S_N2' nucleophilic ring-opened product **17** as a mixture of diastereomers (eq 9).[27] No trace of the base-induced product was detected in the crude ^1H NMR. The reaction was fast and clean, showing again the importance of an electron-withdrawing group on the nitrogen atom in the nucleophilic ring-opening reaction. It is important to note that several signals of the ^{13}C spectra of **16** and **17** were doubled or broaden, and that the ^1H NMR spectra were not resolved due to the slow interconversion of rotational isomers attributable to the carbamate moiety.



16 **17**

Conclusion

We have described a chemo-, regio-, and stereocontrolled methodology for the simple and efficient synthesis of a large variety of polycyclic systems with control at up to six stereocenters. We have established that the most useful feature of the reactivity of the dioxacyclic compounds toward the nucleophilic ring-opening reaction is that the first ring-opening reaction is significantly faster than the second allowing the sequential transformation of the oxabicyclic moieties. The flexibility of the sequential ring-opening process and its limitations have been demonstrated and a new enantioselective mode of opening was reported. The enantioselective base-induced desymmetrization was successfully applied to thiadioxapentacycle in >95% ee using a chiral lithium amide base. Studies are in progress in the application of this process to the synthesis of natural products.

Experimental Section

The following includes general experimental procedures, specific details for representative reactions, and isolation and spectroscopic information for the compounds prepared.

General Procedure for the $LiAlH(OMe)_3$ Reduction of Diacid and Diester. *exo,exo*-2,7-Bis(hydroxymethyl)-11,12-dioxatetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodeca-4,9-diene (2a). Anhydrous MeOH (16.71 mL, 412.56 mmol) was *carefully* added to a suspension of $LiAlH_4$ (5.22 g, 137.52 mmol) in THF (250 mL) at 0 °C. After the addition was complete, the mixture was stirred for 15 min at rt. The diacid **1a**[3] (2.50 g, 9.99 mmol) was added portionwise, and the mixture was heated at reflux for 12 h. The reaction was cooled to rt, and transferred into a large Erlenmeyer flask (1 L), further diluted with THF (250 mL), and quenched by the portionwise addition of powdered potassium sodium tartrate tetrahydrate (38.8 g, 137.52 mmol), followed by water (5 mL), and stirred for an additional 8 h at rt. The suspension was filtered, and the solid residue was washed several times with boiling THF. The filtrate was concentrated in vacuo and purification by flash chromatography (EtOAc−MeOH 4:1) yielded **2a** (745 mg, 34%) as a white solid: $R_f = 0.12$ on silica gel (EtOAc−MeOH 95:5); mp 203−206 °C (MeOH); IR (KBr) 3501, 3402, 3255, 3002, 2931, 1673 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 6.74 (4H, s), 5.02 (4H, s), 3.16 (4H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 140.7, 85.3, 67.3, 62.2; HRMS calcd for $C_{12}H_{14}O_4$ $[M]^+$ 222.0892, found 222.0897.

General Procedure for the Protection of Diol as DiTBDMS Ether. *exo,exo*-2,7-Bis(*tert*-butyldimethylsiloxy)methyl]-11,12-dioxatetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodeca-4,9-diene (2b). Imidazole (1.07 g, 15.76 mmol) and TBDMSCl (1.90 g, 12.61 mmol) were successively added to a solution of **2a** (700 mg, 3.15 mmol) in DMF (4 mL), and the mixture was stirred for 24 h at rt. The reaction was diluted with water, and the resulting solution was extracted (4×) with hexanes−CH_2Cl_2 9:1. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Purification by flash chromatography (hexanes−EtOAc 5:1) yielded **2b** (1.27 g, 89%) as a white solid: $R_f = 0.34$ on silica gel (hexanes−EtOAc 4:1); mp 149−152 °C (Et_2O); IR (KBr) 3002, 2945, 2889, 1469 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.62 (4H, s), 5.04 (4H, s), 3.13 (4H, s), 0.90 (18H, s), 0.01 (12H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 139.9, 84.2, 67.7, 61.2, 25.7, 18.0, −5.6. Anal. Calcd for $C_{24}H_{42}O_4Si_2$: C, 63.95; H, 9.39. Found: C, 63.93; H, 9.40.

Diol 4a. The reaction was carried out as in the general procedure using MeOH (10.05 mL, 248.16 mmol), $LiAlH_4$ (3.47 g, 82.72 mmol), and **3b**[3] (1.50 g, 5.17 mmol) in THF (100 mL). The reaction was quenched with powdered potassium sodium tartrate tetrahydrate (23.40 g, 82.72 mmol). Purification by flash chromatography (EtOAc−MeOH 95:5) yielded **4a** (990 mg, 73%) as a white solid: $R_f = 0.17$ on silica gel (MeOH−EtOAc 95:5); mp 138−141 °C (MeOH); IR (KBr) 3452, 3402, 3072, 3001, 2966, 1638, 1447 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 6.67 (2H, dd, $J = 5.5$, 1.8 Hz), 6.55 (2H, d, $J = 5.5$ Hz), 4.94 (2H, d, $J = 1.8$ Hz), 3.24 (2H, s), 3.14 (2H, s), 2.42 (2H, td, $J = 13.6$, 4.5 Hz), 2.02−1.96 (2H, m), 1.91 (1H, qt, $J = 13.6$, 4.2 Hz), 1.67−1.61 (1H, m); ^{13}C NMR (100 MHz, CD_3OD) δ 143.5, 140.4, 91.9, 84.3, 66.7, 66.6, 65.4, 57.9, 27.7, 18.5. Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.30; H, 6.83.

General Procedure for the Nucleophilic Alkyllithium Ring-Opening. (1*R,2*R**,7*S**,8*S**)-4a,8a-Bis[(*tert*-butyldimethylsiloxy)methyl]-2,7-dibutyl-1,2,4a,7,8,8a-hexahydronaphthalene-1,8-diol (5a) and (1*R**,2*R**,4a*S**,5*R**,6*R**,8a*S**)-4a,8a-Bis[(*tert*-butyldimethylsiloxy)methyl]-2,6-dibutyl-1,2,4a,5,6,8a-hexahydronaphthalene-1,5-diol (5b).** A solution of *n*-BuLi (1.07 mL, 2.5 M solution in hexanes, 2.66 mmol) was added dropwise to a solution of **2b** (100 mg, 0.22 mmol) in Et_2O (10 mL) at −78 °C. After the addition was complete, the mixture was stirred for 8 h at 0 °C. The reaction was quenched with a saturated NH_4Cl solution. The aqueous layer was extracted (3×) with Et_2O, and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Purification by flash chromatography (hexanes−EtOAc 9:1) yielded **5a** (92 mg) and **5b** (24 mg) as white solids in a 2.9:1 ratio, in a combined yield of 92%. Diol **5a**: $R_f = 0.64$ on silica gel (hexanes−EtOAc 9:1); mp 70−72 °C (Et_2O); IR ($CHCl_3$) 3684, 3620, 3030, 2973, 1483 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.66 (2H, dd, $J = 10.3$, 2.6 Hz), 5.23 (2H, dd, $J = 9.9$, 2.6 Hz),

(25) This reaction has been recently used for the enantioselective desymmetrization of aza- and thiaoxabicyclo[3.2.1] and [3.3.1] systems for the synthesis of azepines, thiepines, and thiocines: Lautens, M.; Fillion, E.; Sampat, M. *J. Org. Chem.* **1997**, *62*, 7080.

(26) Olofson, R. A.; Martz, J. T.; Senet, J.-P.; Piteau, M.; Malroof, T. *J. Org. Chem.* **1984**, *49*, 2081.

(27) (a) For an excellent review on enantioselective deprotonation: Beak, P.; Basu, A.; Gallagher, D. J.; Park, Y. S.; Thayumanavan, S. *Acc. Chem. Res* **1996**, *29*, 552. (b) For examples of deprotonation−elimination, see: (b) Beak, P.; Lee, W. K. *J. Org. Chem.* **1993**, *58*, 1109. (c) Garrido, F.; Mann, A.; Wermuth, C.-G. *Tetrahedron Lett.* **1997**, *38*, 63.

4.57 (2H, t, J = 5.2 Hz), 3.90 (2H, s), 3.28 (2H, s), 2.86 (2H, d, J = 4.8 Hz), 2.32−2.26 (2H, m), 1.83−1.74 (2H, m), 1.49−1.24 (10H, m), 0.91−0.88 (6H, m), 0.90 (9H, s), 0.85 (9H, s), 0.07 (6H, s), −0.01 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 130.7, 128.6, 70.3, 70.1, 67.2, 45.5, 44.4, 38.9, 30.6, 29.8, 25.9, 25.8, 23.0, 18.2, 18.1, 14.3, −5.5, −5.7; HRMS calcd for $C_{32}H_{62}O_4Si_2$ 566.4186, found 566.4173. Diol **5b**: R_f = 0.27 on silica gel (hexanes−EtOAc 9:1); mp 95−97 °C (Et_2O); IR ($CHCl_3$) 3684, 3620, 3023, 2966, 2931, 1483, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.65 (2H, dd, J = 10.3, 2.6 Hz), 5.57 (2H, d, J = 2.6 Hz), 3.91 (2H, d, J = 3.3 Hz), 3.65 (2H, bs), 3.61 (2H, d, J = 9.5 Hz), 3.41 (2H, d, J = 9.6 Hz), 2.23 (2H, m), 1.61−1.52 (2H, m), 1.42−1.24 (10H, m), 0.88 (6H, t, J = 6.6 Hz), 0.87 (18H, s), 0.01 (6H, s), 0.00 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 130.0, 129.0, 69.1, 65.7, 46.9, 36.6, 31.1, 29.4, 25.8, 22.9, 18.1, 14.1, −5.5, −5.6; HRMS calcd for $C_{32}H_{62}O_4Si_2$ 566.4186, found 566.4207.

(1*S,2*R**,3*R**,4*R**,7*S**,8*R**)-4-Butyl-2,7-bis[(*tert*-butyldimethylsiloxy)methyl]-11-oxatricyclo[6.2.1.0^{2,7}]undeca-5,9-dien-3-ol (5c).** The reaction was carried out as in the general procedure using *n*-BuLi (767 μL, 2.5 M solution in hexanes, 1.92 mmol) and **2b** (173 mg, 0.38 mmol) in Et_2O (7 mL) at −78 °C for 4 h. Purification by flash chromatography (hexanes−EtOAc 7:1) yielded **5c** as a colorless oil (178 mg, 91%): R_f = 0.51 on silica gel (hexanes−EtOAc 7:1); IR (neat) 3536, 3086, 3016, 2945, 1469 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.54 (1H, dd, J = 5.9, 1.8 Hz), 6.45 (1H, dd, J = 5.9, 1.5 Hz), 5.84 (1H, dd, J = 9.5, 2.9 Hz), 5.59 (1H, dd, J = 9.9, 1.8 Hz), 5.02 (1H, t, J = 1.3 Hz), 4.47 (1H, t, J = 1.3 Hz), 4.11 (1H, dt, J = 11.0, 1.3 Hz), 3.49 (1H, d, J = 10.3 Hz), 3.29 (1H, d, J = 9.5 Hz), 3.22 (1H, d, J = 10.3 Hz), 3.14 (1H, d, J = 9.5 Hz), 2.76 (1H, d, J = 10.6 Hz), 2.20−2.14 (1H, m), 1.64−1.19 (6H, m), 0.89−0.87 (3H, m), 0.88 (9H, s), 0.84 (9H, s), 0.01 (3H, s), 0.00 (3H, s), −0.04 (3H, s), −0.05 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 135.8, 134.0, 133.2, 84.8, 83.9, 71.1, 66.2, 64.0, 54.0, 51.8, 38.4, 31.3, 29.6, 25.8, 25.7, 22.8, 18.2, 18.1, 14.1, −5.5 (2), −5.6, −5.7; HRMS calcd for $C_{28}H_{52}O_4Si_2$ [M − Bu]$^+$ 451.2700, found 451.2701.

Procedure for the Opening of 5c Using (*i*-Bu)$_3$Al/*n*-BuLi. A solution of **5c** (50 mg, 0.10 mmol) in Et_2O (5 mL) was treated with (*i*-Bu)$_3$Al (27 μL, 0.11 mmol) at 0 °C, and the mixture was stirred for 30 min. The solution was cooled to −78 °C prior to the addition of *n*-BuLi (275 uL, 2.5 M solution in hexanes, 0.69 mmol). After the addition was complete, the mixture was stirred for 10 min at −78 °C, and 48 h at −78 °C.

(1*R,2*R**,4a*S**,5*R**,6*R**,8a*S**)-4a,8a-Bis[(*tert*-butyldimethylsiloxy)methyl]-2,6-dibutyl-4,8-dimethyl-1,2,4a,5,6,8a-hexahydronaphthalene-1,5-diol (6a).** The reaction was carried out as in the general procedure using *n*-BuLi (500 μL, 2.5 M solution in hexanes, 1.25 mmol) and **2d** (50 mg, 0.10 mmol) in Et_2O (3 mL) at 0 °C for 7 h. Purification by flash chromatography (hexanes−EtOAc 9:1) yielded **6a** as a white solid (55 mg, 90%): R_f = 0.74 on silica gel (hexanes−EtOAc 6:1); mp 138−140 °C (Et_2O); IR (KBr) 3416, 3262, 2959, 2931 1469 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (2H, d, J = 1.1 Hz), 3.98 (2H, d, J = 3.3 Hz), 3.76 (2H, d, J = 10.2 Hz), 3.62 (2H, bs), 3.56 (2H, d, J = 10.3 Hz), 2.16−2.05 (2H, m), 1.80 (6H, dd, J = 2.4, 1.3 Hz), 1.52−1.47 (2H, m), 1.39−1.28 (10H, m), 0.89 (6H, t, J = 6.9 Hz), 0.86 (18H, s), 0.01 (12H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 134.3, 127.6, 68.4, 65.7, 50.5, 36.5, 31.7, 29.5, 25.9, 23.1, 21.0, 18.0, 14.2, −5.6, −5.8. Anal. Calcd for $C_{34}H_{66}O_4Si_2$: C, 68.63; H, 11.18. Found: C, 68.60; H, 11.28.

(1*S,2*R**,3*R**,4*R**,7*S**,8*R**)-2,7-Bis(methoxymethyl)-1,4,6-trimethyl-11-oxatricyclo[6.2.1.0^{2,7}]undeca-5,9-dien-3-ol (7a).** The reaction was carried out as in the general procedure using MeLi (7.70 mL, 1.4 M solution in Et_2O, 10.79 mmol) and **2e** (600 mg, 2.16 mmol) in Et_2O (25 mL) at rt for 24 h. Purification by flash chromatography (hexanes−EtOAc 2:1) yielded **7a** (253 mg, 40%) as a white solid: R_f = 0.55 on silica gel (hexanes−EtOAc 2:1); mp 49−52 °C (Et_2O); IR (neat) 3529, 3079, 2973, 2924, 1455 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.36 (1H, dd, J = 5.9, 1.9 Hz), 6.28 (1H, d, J = 5.8 Hz), 5.35 (1H, q, J = 1.6 Hz), 4.79 (1H, d, J = 1.8 Hz), 4.05 (1H, dd, J = 11.0, 1.5 Hz), 3.41 (1H, d, J = 9.9 Hz), 3.24 (3H, s), 3.18 (1H, d, J = 9.6 Hz), 3.15 (3H, s), 3.02 (1H, d, J = 9.9 Hz), 3.88−3.85 (2H, m), 2.36−2.23 (1H, m), 1.89 (3H, dd, J = 2.2, 1.5 Hz), 1.80 (3H, s), 1.10 (3H, d, J = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.1, 137.2, 135.2, 131.2, 92.1, 80.2, 74.4 (2), 71.4, 59.2, 58.9, 55.2, 54.3, 32.5, 20.1, 18.2, 17.5; HRMS calcd for $C_{17}H_{26}O_4$ [M]$^+$ 294.1831, found 294.1842.

General Procedure for the Nickel-Catalyzed DIBAL-H Ring-Opening. (1*R,4a*S**,5*R**,6*R**,8a*S**)-5-Methoxy-4a,8a-bis(methoxymethyl)-4,6,8-trimethyl-1,2,4a,5,6,8a-hexahydronaphthalen-1-ol (7c).** $Ni(COD)_2$ (12 mg, 0.04 mmol) was dissolved in dry toluene (3 mL) and transferred via cannula into a flask containing 1,4-bis(diphenylphosphino)-butane (dppb) (37 mg, 0.09 mmol). The mixture was stirred at rt for 30 min and transferred into a flask containing the substrate **7b** (70 mg, 0.23 mmol) in toluene (3 mL). DIBAL-H (250 μL, 1.0 M in hexanes, 0.25 mmol) was added over 1 h via syringe pump. After the addition was complete, the mixture was stirred for an additional 30 min at rt. The reaction was quenched with a saturated NH_4Cl solution. The aqueous layer was extracted (3×) with Et_2O, and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Purification by flash chromatography (hexanes−EtOAc 3:1) gave **7c** (55 mg, 78%) as a white solid: R_f = 0.35 on silica gel (hexanes−EtOAc 3:1); mp 100−102 °C (Et_2O); IR (KBr) 3311, 2959, 2917, 1462 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.24 (1H, d, J = 10.2 Hz), 5.56 (1H, m), 5.29 (1H, d, J = 1.1 Hz), 3.68 (1H, dd, J = 10.3, 2.6 Hz), 3.55 (2H, dd, J = 9.2, 1.5 Hz), 3.42 (4H, bs), 3.27 (1H, d, J = 9.2 Hz), 3.23−3.21 (1H, m), 3.21 (6H, s), 2.26−2.17 (1H, m), 2.14−2.10 (2H, m), 1.84 (3H, m), 1.76 (3H, dd, J = 2.4, 1.3 Hz), 1.02 (3H, d, J = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.8, 133.2, 127.3, 123.2, 83.1, 75.2, 75.1, 67.5, 61.0, 58.6 (2), 49.2 (2), 31.6, 31.3, 20.2, 19.0, 17.2. Anal. Calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.89; H, 9.70.

General Procedure for the Sequential Palladium-Catalyzed Hydrostannation/Tin−Lithium Exchange Ring-Opening. (1*S,4a*R**,5*S**,8a*R**)-4a,8a-Bis[(*tert*-butyldimethylsiloxy)methyl]-1,5-dimethyl-1,2,4a,5,6,8a-hexahydronaphthalene-1,5-diol (7d).** Bu_3SnH (250 μL, 0.93 mmol) was added dropwise over 3 h using a syringe pump to a suspension of $Pd(OH)_2$ on carbon (5 mg, 0.04 mmol) and **2d** (111 mg, 0.23 mmol) in THF (5 mL) at rt. After the addition was complete, the mixture was stirred for an additional 30 min. Et_2O (20 mL) was poured into the reaction mixture, and the resulting solution was filtered through a pad of Celite. The filtrate was concentrated, and the residue was purified by flash chromatography (100% hexanes followed by hexanes−EtOAc 15:1) to give the dihydrostannylated product as a colorless oil. The latter was dissolved in THF (5 mL) and treated with *n*-BuLi (835 μL, 2.5 M solution in hexanes, 2.09 mmol) at 0 °C. The mixture was stirred for 1 h at 0 °C and quenched a saturated NH_4Cl solution. The aqueous layer was extracted (3×) with Et_2O, and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Purification by flash chromatography (hexanes−EtOAc 3:1) gave **7d** (28 mg, 25%) as a white powder: R_f = 0.26 on silica gel (hexanes−EtOAc 3:1); mp 224−225 °C (CH_2Cl_2); IR (KBr) 3231, 3136, 2927, 2855, 1471 cm^{-1}; ^{1}H NMR (400 MHz, toluene-d_8, 70 °C) δ 5.90−5.85 (2H, m), 5.71 (2H, ddd, J = 10.6, 5.2, 3.0 Hz), 4.16 (2H, d, J = 10.6 Hz), 3.97−3.95 (4H, m), 2.46 (2H, d, J = 1.1 Hz), 2.06−2.04 (2H, m), 1.49 (6H, s), 0.90 (18H, s), 0.05 (6H, s), 0.04 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 127.9, 127.0, 75.5, 64.6, 49.0, 37.6, 26.8, 25.7, 18.0, −5.5, −5.6; HRMS calcd for $C_{26}H_{50}O_4Si_2$ [M − OH]$^+$ 465.3220, found 465.3198.

(1*R,2*R**,4a*S**,5*R**,6*R**,8a*R**)-*N*-[4a,8a-Bis[(*tert*-butyldimethylsiloxy)methyl]-2,6-dibutyl-5-hydroxy-4,8-dimethyl-1,2,4a,5,6,8a-hexahydronaphthalen-1-yl]-4-methylbenzenesulfonamide (8a).** The reaction was carried out as in the general procedure using *n*-BuLi (1.52 mL, 2.5 M solution in hexanes, 3.80 mmol) and **2g** (200 mg, 0.32 mmol) in Et_2O (7 mL) at 0 °C for 1 h. Purification by flash chromatography (hexanes−EtOAc 7:1) yielded **8a** (218 mg, 92%) as a white crystalline solid: R_f = 0.46 on silica gel (hexanes−EtOAc 6:1); mp 205−207 °C (Et_2O); IR (KBr) 3402, 2966, 2931, 1469 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (1H, br d, J = 8.1 Hz), 7.64 (2H, d, J = 8.6 Hz), 7.13 (2H, d, J = 8.0 Hz), 5.47 (1H, bs),

4.86 (1H, bs), 4.11−4.08 (2H, m), 3.72 (1H, d, J = 10.2 Hz), 3.64 (1H, d, J = 10.3 Hz), 3.51 (1H, d, J = 10.3 Hz), 3.48 (1H, d, J = 10.3 Hz), 2.37 (3H, s), 2.22−2.00 (3H, m), 1.77 (3H, bs), 1.46 (3H, d, J = 0.8 Hz), 1.42−1.13 (12H, m), 0.93−0.80 (6H, m), 0.88 (9H, s), 0.84 (9H, s), 0.01 (3H, s), 0.00 (3H, s), −0.01 (3H, s), −0.02 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3, 141.0, 134.9, 133.8, 129.0, 128.5, 126.6 (2), 69.2, 65.9, 65.4, 54.4, 50.22, 50.19, 36.6, 35.9, 32.3, 30.8, 29.7, 29.4, 25.84, 25.81, 23.0, 22.9, 21.8, 21.4, 20.7, 17.92, 17.89, 14.19, 14.13, −5.6, −5.7, −5.9, −6.0. Anal. Calcd for $C_{41}H_{73}NO_5SSi_2$: C, 65.81; H, 9.83; N, 1.87. Found: C, 65.71; H, 9.76; N, 1.88.

(1*S,2*S**,3*R**,4*R**,7*S**,8*R**)-*N*-[2,7-Bis[(*tert*-butyldimethylsiloxy)methyl]-4-butyl-1,6-dimethyl-11-oxatricyclo-[6.2.1.0^{2,7}]undeca-5,9-dien-3-yl]-4-methylbenzenesulfonamide (8b).** The reaction was carried out as in the general procedure: *n*-BuLi (127 μL + 64 μL + 64 μL, 2.5 M solution in hexanes, 0.64 mmol) was added in three portions to a solution of **2g** (100 mg, 0.16 mmol) in Et_2O (10 mL) at −78 °C over 20 min. After the addition was complete, the mixture was stirred for an additional 10 min at −78 °C. Purification by flash chromatography (hexanes−EtOAc 5:1) yielded **8b** (89 mg, 82%) as a white solid: R_f = 0.33 on silica gel (hexanes−EtOAc 5:1); mp 125−128 °C (Et_2O); IR (KBr) 3743, 3445, 3417, 3290, 2952, 2931, 1469 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (2H, d, J = 8.4 Hz), 7.19 (2H, d, J = 8.5 Hz), 6.33 (1H, dd, J = 5.7, 1.7 Hz), 6.28 (1H, d, J = 5.5 Hz), 5.51 (1H, d, J = 7.3 Hz), 5.29 (1H, bs), 4.71 (1H, d, J = 1.8 Hz), 4.47 (1H, d, J = 7.3 Hz), 3.91 (1H, d, J = 10.6 Hz), 3.33 (1H, d, J = 11.0 Hz), 3.31 (1H, d, J = 10.2 Hz), 3.04 (1H, d, J = 10.3 Hz), 2.36 (3H, s), 2.12−2.09 (1H, m), 1.83 (3H, s), 1.82 (3H, s), 1.23−0.82 (6H, m), 0.94 (9H, s), 0.78 (9H, s), 0.73 (3H, t, J = 7.2 Hz), 0.05 (3H, s), 0.03 (3H, s), −0.08 (3H, s), −0.10 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.5, 141.7, 141.6, 136.4, 134.8, 132.6, 129.0, 126.1, 91.9, 80.0, 65.5, 62.8, 58.0, 56.3, 55.6, 38.3, 31.9, 29.9, 25.9, 25.6, 22.6, 21.4, 19.5, 19.0, 18.2, 18.0, 13.9, −5.6, −5.7, −5.8, −5.9; HRMS calcd for $C_{37}H_{63}NO_5SSi_2$ [M]$^+$ 689.3966, found 689.3952.

(1*R,2*R**,4a*S**,5*R**,6*S**,8a*R**)-*N*-[4a,8a-Bis[(*tert*-butyldimethylsiloxy)methyl]-2-butyl-6-*tert*-butyl-5-hydroxy-4,8-dimethyl-1,2,4a,5,6,8a-hexahydronaphthalen-1-yl]-4-methylbenzenesulfonamide (8c).** The reaction was carried out as in the general procedure using *tert*-BuLi (1.79 mL, 1.7 M solution in pentane, 3.05 mmol) and **8b** (300 mg, 0.44 mmol) at 0 °C for 30 min. Purification by flash chromatography (hexanes−EtOAc 7:1) yielded **8c** (306 mg, 94%) as a white solid: R_f = 0.43 on silica gel (hexanes−EtOAc 7:1); mp 185−187 °C (Et_2O); IR (KBr) 3432, 3054, 2955, 2930, 1469 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (2H, d, J = 8.4 Hz), 7.15 (2H, d, J = 8.1 Hz), 5.48 (1H, bs), 5.34 (1H, bs), 4.26−4.23 (2H, m), 3.77 (1H, d, J = 10.2 Hz), 3.62 (1H, d, J = 10.3 Hz), 3.56 (1H, d, J = 10.2 Hz), 3.50 (1H, d, J = 9.9 Hz), 2.35 (3H, s), 2.09 (1H, bs), 1.82 (1H, bs), 1.76 (3H, d, J = 1.1 Hz), 1.67 (3H, d, J = 1.5 Hz), 1.35−1.10 (6H, m), 1.06−0.93 (2H, m), 0.99 (9H, s), 0.89 (9H, s), 0.86 (9H, s), 0.81 (3H, t, J = 7.2 Hz), 0.01 (6H, s), 0.00 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 140.9, 136.1, 133.6, 130.0, 128.8, 126.6, 124.1, 69.3, 66.1, 65.4, 54.0, 51.0, 50.3, 44.3, 36.8,33.0,32.4, 29.7, 28.5, 25.9, 25.8, 22.8, 21.7, 21.4, 20.8, 17.9, 14.1, −5.6, −5.7, −5.86, −5.94. Anal. Calcd for $C_{41}H_{73}NO_5SSi_2$: C, 65.81; H, 9.83; N, 1.87. Found: C, 66.15; H, 9.86; N, 1.97.

Iodide 9a. A solution of **2i** (563 mg, 1.04 mmol) and NaI (781 mg, 5.21 mmol) in acetone (40 mL) was heated at reflux for 48 h. The solvent was removed in vacuo, and the resulting solid was washed several times with Et_2O. After concentration of the filtrate, the residue was purified by flash chromatography (hexanes−EtOAc 7:1) to give **9a** (586 mg, 89%) as a pale yellow oil: R_f = 0.41 on silica gel (hexanes−EtOAc 7:1); IR (neat) 3073, 3009, 2909, 1462 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.60−6.57 (2H, m), 6.44 (1H, d, J = 4.4 Hz), 6.43 (1H, d, J = 5.4 Hz), 5.04 (1H, d, J = 1.5 Hz), 5.02 (1H, d, J = 1.8 Hz), 3.34−3.29 (1H, m), 3.20 (1H, d, J = 10.2 Hz), 3.18 (1H, d, J = 9.8 Hz), 3.15−3.09 (1H, m), 3.09 (1H, d, J = 10.3 Hz), 3.07 (1H, d, J = 10.2 Hz), 2.44 (1H, ddd, J = 14.0, 11.2, 4.4 Hz), 2.18−2.08 (1H, m), 2.02−1.95 (1H, m), 1.93−1.82 (1H, m), 1.70 (3H, s), 0.91 (9H, s), 0.89 (9H, s), 0.05 (3H, s), 0.02 (3H, s), 0.01 (3H, s), 0.00 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 141.7, 140.6, 140.0, 93.4, 90.5, 80.3 (2), 67.6, 67.5, 64.3, 63.9, 31.3, 29.4, 26.0, 25.8, 18.2, 18.1, 16.5, 7.6, −5.3, −5.5, −5.6, −5.7. Anal. Calcd for $C_{28}H_{49}IO_4Si_2$: C, 53.15; H, 7.81. Found: C, 53.12; H, 7.96.

Alcohol 9b. A solution of *tert*-BuLi (499 μL, 1.7 M solution in pentane, 0.85 mmol) was added dropwise to a solution of **9a** (244 mg, 0.39 mmol) in pentane−Et_2O 3:2 (5.0 mL) at −78 °C. After the addition was complete, the mixture was stirred at −78 °C for 2 h. Purification by flash chromatography (CH_2Cl_2−EtOAc 95:5) gave **9b** (147 mg, 75%) as a white solid: R_f = 0.57 on silica gel (CH_2Cl_2−EtOAc 95:5); mp 84−87 °C (Et_2O); IR (neat) 3438, 2953, 2930, 1467 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (1H, d, J = 4.8 Hz), 6.27 (1H, d, J = 5.5 Hz), 5.93−5.91 (1H, m), 5.86 (1H, dd, J = 9.9, 1.5 Hz), 4.83 (1H, bs), 3.79 (1H, bs), 3.43−3.35 (4H, m), 2.52 (1H, bs), 1.96−1.65 (6H, s), 1.56 (3H, s), 0.87 (9H, s), 0.84 (9H, s), −0.01 (3H, s), −0.02 (3H, s), −0.03 (3H, s), −0.04 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6, 136.4, 132.3, 129.8, 89.2, 82.2, 82.1, 68.2, 63.5, 56.6, 54.0, 43.8, 34.2, 26.2, 25.9, 25.8, 21.5, 18.2, 17.9, 17.0, −5.5, −5.6, −5.8, −5.9. Anal. Calcd for $C_{28}H_{50}O_4Si_2$: C, 66.35; H, 9.94. Found: C, 66.61; H, 9.96.

General Procedure for the Nucleophilic Alkylmagnesium Chloride/Alkyllithium Ring-Opening. (1*R,2*R**,8*S**,9*S**,9a*S**,9b*S**)-9a,9b-Bis[(*tert*-butyldimethylsiloxy)-methyl]-2,8-dibutyl-2,4,5,6,8,9,9a,9b-octahydro-1*H*-phenalene-1,9-diol (11c).** A solution of *n*-BuMgCl (137 μL, 2.0 M solution in Et_2O, 0.27 mmol) was added dropwise to a solution of the alcohol **11a** (75 mg, 0.14 mmol) in Et_2O (3 mL) at 0 °C. The mixture was stirred 30 min at 0 °C, and *n*-BuLi (273 μL, 2.5 M solution in hexanes, 0.68 mmol) was added dropwise. The mixture was stirred for an additional 30 min at 0 °C after which time the solution turned cloudy. THF (3 mL) was added, and the mixture was stirred for 12 h at rt. The reaction was quenched by the addition of a saturated NH_4-Cl solution. The aqueous layer was extracted (3×) with Et_2O, and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Purification by flash chromatography (hexanes−EtOAc 15:1) yielded **11c** (65 mg, 78%) as a clear oil: R_f = 0.81 on silica gel (hexanes−EtOAc 9:1); IR (neat) 3571, 3508, 2966, 1666, 1462 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.41 (2H, bs), 4.56 (2H, d, J = 5.5 Hz), 3.99 (2H, s), 3.66 (2H, s), 2.98 (2H, bs), 2.35−2.16 (6H, m), 1.87−1.71 (4H, m), 1.51−1.23 (10H, m), 0.90−0.87 (6H, m), 0.89 (9H, s), 0.85 (9H, s), 0.06 (6H, s), 0.01 (6H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 136.9, 127.2, 70.9, 70.5, 62.8, 48.9, 46.3, 38.6, 33.1, 30.7, 30.1, 29.4, 25.8 (2), 23.1, 18.0 (2), 14.3, −5.6, −5.7. Anal. Calcd for $C_{35}H_{66}O_4$-Si_2: C, 69.25; H, 10.96. Found: C, 69.53; H, 10.60.

Alcohol 12a and Alcohol 12b. The reaction was carried out as in the general procedure using *n*-BuLi (1.02 mL, 2.5 M solution in hexanes, 2.54 mmol), and **4e** (250 mg, 0.51 mmol) in Et_2O (15 mL) at −78 °C for 10 min. Purification by flash chromatography (hexanes−EtOAc 7:1) yielded **12a** (140 mg) and **12b** (96 mg) as white solids in a 1.6:1 ratio, in a combined yield of 84%. Alcohol **12a**: R_f = 0.34 on silica gel (hexanes−EtOAc 5:1); mp 69−72 °C (Et_2O); IR (CH_2Cl_2) 3530, 3053, 2955, 2930, 1467 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.61 (1H, dd, J = 5.9, 1.9 Hz), 6.09 (1H, d, J = 5.9 Hz), 5.54 (1H, bs), 5.06 (1H, d, J = 1.8 Hz), 4.22−4.18 (2H, m), 4.11−4.08 (2H, m), 4.00 (1H, d, J = 13.1 Hz), 3.75 (1H, d, J = 10.2 Hz), 3.62 (1H, d, J = 10.3 Hz), 3.29 (1H, d, J = 10.3 Hz), 3.19 (1H, d, J = 10.2 Hz), 2.73−2.68 (1H, m), 2.23−2.18 (1H, m), 1.66−1.18 (6H, m), 0.91−0.87 (3H, m), 0.89 (9H, s), 0.81 (9H, s), 0.01 (3H, s), 0.00 (3H, s), −0.04 (3H, s), −0.06 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 135.8, 134.1, 132.0, 87.0, 83.2, 72.3, 69.0, 67.0, 64.2, 63.3, 55.4, 51.0, 37.2,31.3, 29.6, 25.9, 25.7, 22.8, 18.2, 18.1, 14.2, −5.5, −5.56, −5.59, −5.7; HRMS calcd for $C_{30}H_{54}O_5$-Si_2 [M]$^+$ 550.3510, found 550.3523. Alcohol **12b**: R_f = 0.63 on silica gel (hexanes−EtOAc 5:1); mp 104−107 °C (Et_2O); IR (KBr) 3501, 3030, 2959, 2931, 1469 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 (1H, dd, J = 5.5, 1.8 Hz), 6.32 (1H, d, J = 5.5 Hz), 6.21 (1H, dd, J = 10.1, 2.7 Hz), 5.63 (1H, dd, J = 10.1, 1.7 Hz), 4.92 (1H, d, J = 1.8 Hz), 4.71 (1H, d, J = 1.8 Hz), 4.38 (1H, d, J = 12.4 Hz), 4.25 (1H, d, J = 11.3 Hz), 4.19 (1H, d, J = 12.4 Hz), 4.03 (1H, d, J = 9.9 Hz), 3.91 (1H, dd, J =

10.1, 1.8 Hz), 3.72 (1H, d, J = 9.2 Hz), 3.51 (1H, d, J = 9.2 Hz), 3.23 (1H, d, J = 11.4 Hz), 2.98−2.95 (1H, m), 1.46−1.12 (6H, m), 0.90−0.86 (3H, m), 0.89 (9H, s), 0.84 (9H, s), 0.02 (3H, s), 0.00 (3H, s), −0.02 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.3, 136.3, 132.7, 132.4, 91.2, 84.9, 73.6, 71.2, 71.0, 65.8, 65.3, 52.2, 51.9, 42.1, 30.0, 27.5, 25.9, 25.8, 23.2, 18.2, 18.0, 14.1, −5.4, −5.5, −5.7, −5.9. Anal. Calcd for $C_{30}H_{54}O_5Si_2$: C, 67.36; H, 10.18. Found: C, 66.96; H, 10.11.

Procedure for the Enantioselective Desymmetrization of 4m. Alcohol 15a. A solution of (−)-bis[(*S*)-1-phenylethyl]amine hydrochloride (155 mg, 0.59 mmol) in THF (5 mL) was treated with *n*-BuLi (472 μL, 2.5 M in hexanes, 1.18 mmol) at 0 °C. After the addition was complete, the mixture was stirred for 20 min and cooled to −78 °C prior to the rapid addition of the thiadioxapentacycle **4m** (100 mg, 0.20 mmol) as a solid. The mixture turned magenta after few minutes. The solution was stirred for an additional 5 h at −78 °C. The dry ice−acetone bath was removed, and the mixture was allowed to warm. Immediately after the magenta color disappeared, the reaction was quenched by the addition of a saturated aqueous NH_4Cl solution. Purification by flash chromatography (hexanes−EtOAc 7:1) (two purifications were necessary to remove the excess base) gave (+)-**15a** (73 mg, 73%): >95% ee, $[\alpha]^{22}_D$ = +158° (*c* 1.32, $CHCl_3$): R_f = 0.38 on silica gel (hexanes−EtOAc 7:1); mp 119−121 °C (Et_2O); IR (CCl_4) 3550, 3030, 2959, 1553, 1469 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.61 (1H, dd, J = 5.9, 1.8 Hz), 6.46 (1H, d, J = 9.2 Hz), 6.33 (1H, d, J = 5.8 Hz), 6.15 (1H, dd, J = 9.0, 6.1 Hz), 6.04 (1H, s), 5.04 (1H, d, J = 1.8 Hz), 4.34 (1H, dd, J = 11.0, 5.9 Hz), 3.80 (1H, d, J = 13.6 Hz), 3.31 (1H, d, J = 9.5 Hz), 3.27 (1H, d, J = 9.9 Hz), 3.25 (1H, d, J = 9.5 Hz), 3.13−3.07 (2H, m), 2.84 (1H, d, J = 11.0 Hz), 0.87 (9H, s), 0.85 (9H, s), 0.00 (6H, s), −0.03 (3H, s), −0.04 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 137.8, 134.7, 131.3, 129.1, 116.0, 83.6, 83.5, 66.6, 65.2, 63.9, 58.3, 50.9, 27.0, 25.8 (2), 18.1 (2), −5.5 (2), −5.6, −5.7; HRMS calcd for $C_{26}H_{44}O_4SSi_2$ $[M]^+$ 508.2499, found 508.2516.

Carbamate 16. A solution of **4i** (175 mg, 0.29 mmol) in benzene (3 mL) was treated with 1-chloroethyl chloroformate (34 μL, 0.32 mmol), stirred at rt for 30 min, and heated at reflux for 90 min. The solvent was removed in vacuo and replaced by MeOH (5 mL). The solution was heated at reflux for 1 h. The mixture was cooled to rt prior to the addition of Et_3N (120 μL, 0.85 mmol) and $(BOC)_2O$ (75 mg, 0.34 mmol) and was stirred for an additional 1 h at rt. MeOH was removed in vacuo, and the residue was dissolved in H_2O and extracted (3×) with Et_2O. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Purification by flash chromatography (hexanes−EtOAc 3:1) gave **16** (120 mg, 71%) as a white solid: R_f = 0.43 on silica gel (hexanes−EtOAc 3:1); mp 136−140 °C (Et_2O); IR (neat) 2953, 2930, 1690, 1471 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.66−6.63 (2H, m), 6.47 (2H, d, J = 5.9 Hz), 5.04 (2H, d, J = 1.4 Hz), 4.59 (1H, d, J = 14.2 Hz), 4.46 (1H, d, J = 13.2 Hz), 3.72 (1H, d, J = 14.4 Hz), 3.64 (1H, d, J = 12.9 Hz), 3.24 (2H, s), 3.10 (2H, s), 1.44 (9H, s), 0.89 (9H, s), 0.88 (9H, s), 0.02 (6H, s), 0.01 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 140.8 and 140.6, 140.1, 88.2 and 88.1, 83.6, 79.8, 67.4, 66.4, 63.4, 55.7, 44.9 and 43.8, 28.5, 26.0, 25.8, 18.2, 18.1, −5.4, −5.5. Anal. Calcd for $C_{31}H_{53}NO_6Si_2$: C, 62.90; H, 9.02; N, 2.37. Found: C, 63.05; H, 9.02; N, 2.35.

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Supporting Information Available: Experimental details and characterization are available for compounds **2c**−**k**, **4b**−**o**, **6b,c**; **7b**, **9c**, **10**, **11a**,**b**,**d**,**e**−**g**, **12c**−**f**, **13**, **15b**, **17**. ORTEP drawings and details of the data acquisition are available for compounds **8c** and **11f** (35 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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