(m, 2 H), 2.40 (t, $J = 7$ Hz, 2 H), and 5.77 (t, $J = 7$ Hz, 1 H). If the hydrosilation product was isolated by distillation and subjected to the same transformation, isomerically pure ($E > 99\%$) bromide was obtained in 80% yield. The only impurity (ca. 5%) was tentatively assigned to 5-methoxy-5-decene (MS, m/e 170). The use of bromine (do not use in excess amounts) instead of NBS in the one-pot procedure afforded the bromide ($E/Z = 95/5$) in 76% yield, which contained more impurities. NBS is the reagent of choice.

(b) (*E*)-5-Iodo-5-decene. The use of iodine (1.0 molar equiv to the acetylene) at room temperature for 4 h, instead of NBS or bromine in (a), gave the (*E*)-iodide[22a] ($E > 99\%$) in 86% yield: bp 96 °C/18 mmHg; ^{1}H NMR (CCl_4) δ 0.8–1.15 (m, 6 H), 1.15–1.7 (m, 8 H), 2.06 (dt, $J = 7$ and 7 Hz, 2 H), 2.37 (t, $J = 7$ Hz, 2 H), 6.13 (t, $J = 7$ Hz, 1 H). Anal. Calcd for $C_{10}H_{19}I$: 266.0529. Found: 266.0536.

(c) (*Z*)-5-Bromo-5-decene. To the hydrosilation product obtained as above from 5-decyne (414 mg, 2.99 mmol) were added CCl_4 (10 mL) and bromine (0.135 mL; do not use in excess) dropwise at 0 °C. After stirring at 0 °C for 2 h, methanol (10 mL) and KHF_2 (1312 mg, 16.79 mmol) were added, and the mixture was stirred at room temperature overnight. Usual workup gave 544 mg (83% yield) of the *Z* isomer[12] ($Z > 98\%$): bp 88 °C/19 mmHg; ^{1}H NMR (CCl_4) δ 0.8–1.1 (m, 6 H), 1.1–1.7 (m, 8 H), 2.0–2.3 (m, 2 H), 2.40 (t, $J = 7$ Hz, 2 H), and 5.57 (t, $J = 7$ Hz, 1 H); MS, m/e (relative intensity) 218, 220 (M^+, 11), 83 (100).

(d) (*E*)-1-Bromo-3,3-dimethyl-1-butene was obtained in 49% yield by similar procedures to those described in (a) and by careful workup of the highly volatile product; $E/Z = 98/2$, bp 65 °C/122 mmHg (bath temperature). The rather low yield was attributable to the high volatility of the product, since the yield determined by GLC was 86%. ^{1}H NMR were superimposable on the literature data.[5]

Acknowledgment. We thank Mr. K. Matsushita of JEOL for measurements of ^{13}C and ^{19}F NMR spectra and Shin-etsu Chemical Industrial Co., Ltd. for a gift of organosilicon compounds.

The Stereochemistry of S_N2' Addition to Macrocyclic α-Methylenecycloalkylidene Epoxides by Organocopper Reagents

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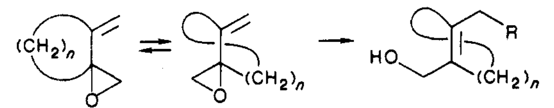
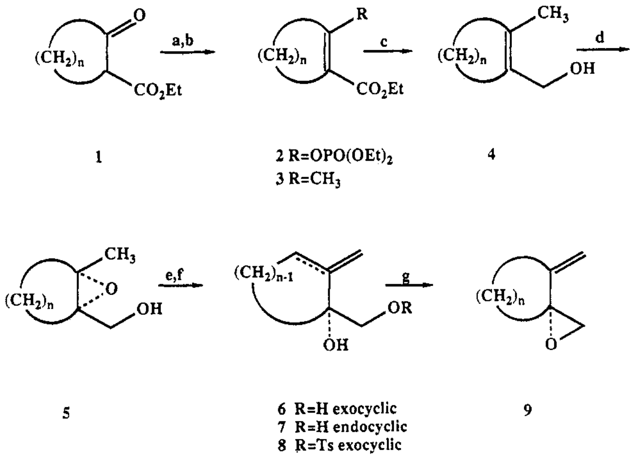
The addition of *n*-butylmagnesium bromide–copper(I) iodide in THF–dimethyl sulfide has been carried out with the 12-, 14-, and 16-membered optically active (*R*)-2-methylenecycloalkylidene epoxides **9a**, **9b**, and **9d**. In each case, the S_N2' substitution products **10** and **11** were formed with the trans predominating by 9:1 or better. The 12- and 14-membered cycloalkylidene epoxides **9a** and **9b** gave the (*R*)-cycloalkenylcarbinols **10a** and **10b** of over 90% optical purity. Accordingly, attack on the double bond must occur syn to the epoxide oxygen via the O-exo s-trans conformer of **9a** and **9b**. The 16-membered cycloalkylidene epoxide **9d** gave racemic cycloalkenylcarbinol **10d** upon treatment with the foregoing organocopper reagent. This result is attributable to racemization of **10d** rather than nonselective S_N2' addition.

Additions of organocopper reagents to α-methylenecycloalkylidene epoxides (I) have been found to proceed via S_N2' displacement to afford predominantly (*Z*)-cycloalkenylcarbinols (II).[1] The regio- and stereochemical preferences of this addition are thought to arise from a reactant-like transition state involving π complexation of the organocopper[2] to the lower energy s-trans conformer[3] of the cycloalkylidene epoxide.[1] The present investigation was undertaken to examine the stereoselectivity of the attack relative to the epoxide oxygen. Previous studies of this nature have employed rigid cycloalkene epoxides with fixed s-cis or, less commonly, s-trans geometries.[4] In these cases a general preference for anti S_N2' attack was noted.



I (s-cis) I (s-trans) II

Scheme I[a,b]



[a] **a** series, $n = 10$; **b** series, $n = 12$; **d** series, $n = 14$. [b] (a) NaH, Et_2O, 0 °C; $ClPO(OEt)_2$; (b) $CH_3Li{\cdot}LiBr$, CuI, Et_2O, –78 to 0 °C; (c) DIBAH, hexane; (d) Ti(O-*i*-Pr)$_4$, (+)-DET, TBHP, CH_2Cl_2, –23 °C, 2–3 h; (e) Et_2AlNR_2, 0 °C–reflux; (f) *p*-TsCl, Et_3N, DMAP, CH_2Cl_2, 0 °C; (g) $PhCH_2NMe_3OH$, Et_2O, 20 °C.

For our approach we planned to use optically active α-methylenecycloalkylidene epoxides of known configuration (e.g., **9**; see Figure 1). Addition of the organocopper reagent as described previously would afford the *trans*-cycloalkenylcarbinols (e.g., **10**). These cycloalkenes are

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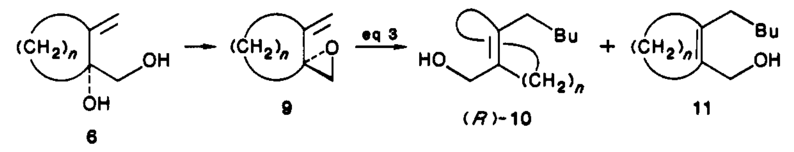
[1] (a) Marshall, J. A.; Flynn, K. E. *J. Am. Chem. Soc.* **1983**, *105*, 3360; **1984**, *106*, 723. (b) Marshall, J. A.; Peterson, J. C.; Lebioda, L. *J. Am. Chem. Soc.* **1983**, *105*, 6515; **1984**, *106*, 6006. (c) Marshall, J. A.; Audia, V. H. *J. Org. Chem.* **1985**, *50*, 1607. (d) Marshall, J. A.; Audia, V. H.; Jenson, T. M.; Guida, W. C. *Tetrahedron* **1986**, *42*, 1703.

[2] Goering, H. L.; Kantner, S. S. *J. Org. Chem.* **1984**, *49*, 422.

[3] Calculations were performed on the 12-membered system I ($n = 10$) by W. Clark Still using his programs Ringmaker-Bakmod-Model. We are indebted to Prof. Still for his valued assistance.

[4] (a) Wender, P. A.; Erhardt, J. M.; Letendre, L. J. *J. Am. Chem. Soc.* **1981**, *103*, 2114. Marino, J. P.; Abe, H. *J. Org. Chem.* **1981**, *46*, 5379. Marino, J. P.; Jaẽn, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 3165. (b) Marino, J. P.; Abe, H. *J. Am. Chem. Soc.* **1981**, *103*, 2907. (c) Ziegler, F. E.; Cady, M. A. *J. Org. Chem.* **1981**, *46*, 122.

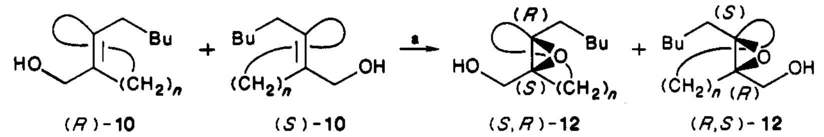
Table I. Stereochemistry of S_N2' Additions of BuMgBr–CuI to Cycloalkylidene Epoxides 9[a]



entry	n	series	6 [α]D	6 ee, %	9 [α]D	9 yield, %	10 [α]D	10 ee, %[c]	10 yield, %	10:11
1	10	a	+26.3	99	−46.1	62	−66.6[b]	92	68	99:1
2	12	b	−14.4	>90	−63.4	72	−113.2[b]	82	59	94:6
3	14	d	−5.3	>90	−54.9	71	−0.4	0	66	89:11

[a] See Scheme I. [b] Corrected for the presence of cis isomer 11. [c] Based on Mosher ester analysis.

Table II. Sharpless Resolutions of *trans*-Cycloalkenylcarbinols 10[a]



entry	series	n	reagent, equiv	recovered (S)-10 [α]D[b]	recovered (S)-10 ee, %	recovered (S)-10 yield, %	epoxide 12 [α]D	epoxide 12 ee, %	epoxide 12 yield, %
1	a	10	0.6	+67.8	98	35	−50.2	56	58
2	b	12	0.6	+133.3	99	40	−66.2	76	31
3	b	12	1.5				−1.0[c]	0	62
4	c	13	0.6	+121.1	90	41	−58.4	66	41
5	c	13	1.5				−0.1[c]	0	55
6	d	14	0.6	+0.7	0	33	−36.3	80	29
7	d	14	1.5				−1.5[c]	0	62

[a] (a) (+)-Diisopropyl tartrate, Ti(O-*i*-Pr)$_4$, *t*-BuOOH, CH_2Cl_2, −20 °C. [b] Corrected for the presence of cis isomer 11. [c] Rotation attributable to cis epoxy alcohol.

chiral, and, depending upon the syn or anti preference of the addition, the *R* or *S* enantiomer could be produced. In the case at hand, syn S_N2' addition to the (*R*)-epoxide 9 would afford the allylic alcohol (*R*)-10 whereas anti addition would give (*S*)-10. The configurations of these allylic alcohols could be ascertained via Sharpless kinetic resolution of the known racemates.[1]

The foregoing analysis is based on the assumption that the bridging methylene chain effectively blocks attack on the double bond from within the ring cavity. The assumption is intuitively reasonable and receives support from the high diastereoselectivity of related Sharpless resolutions.[1a] It should be noted that the two s-trans conformers **9-exo** and **9-endo** (Figure 1) of cycloalkylidene epoxide **9a** (*n* = 10) are calculated to be nearly equal in energy and lower than the s-cis conformer.[3]

The chiral cycloalkylidene epoxides **9a** (*n* = 10), **9b** (*n* = 12), and **9d** (*n* = 14) were prepared as outlined in Scheme I by starting from the appropriate 2-oxocycloalkanecarboxylates **1**. The derived enol phosphates **2** underwent coupling with lithium dimethylcuprate to give the *cis*-cycloalkenecarboxylates **3** as the sole stereoisomers.[5] This point was confirmed upon reduction of the esters with diisobutylaluminum hydride (DIBAH) to the *cis*-cycloalkenylcarbinols **4**. The carbinyl CH_2 grouping of these alcohols was seen as a singlet in the high-field ^1H NMR spectrum. The corresponding trans isomers (e.g., **13**, eq 2), on the other hand, show this methylene as an AB quartet. Sharpless epoxidation[6] was effected with the (+)-diethyl tartrate derived reagent, affording the epoxy alcohols **5** in high optical purity as judged by analysis of the Mosher ester derivatives.[7] Elimination of epoxy alcohols **5** with lithium diethylamide in ether gave the exocyclic allylic alcohols **6** as the major products, contaminated with 15–20% of inseparable endocyclic isomers **7**.[8] Considerably higher regioselectivity was realized with Yamamoto's diethylaluminum 2,2,6,6-tetramethylpiperidide base, whereupon the exocyclic products **6** were produced exclusively.[9] The *p*-toluenesulfonate derivatives **8** readily afforded the highly acid labile epoxides **9** upon treatment with Triton-B hydroxide in ether. The optical purity of these epoxides could not be directly ascertained, but, considering the method of their preparation, it seems safe to assume that they closely approximate those of the diols **6**. These were found to be over 90% optically pure

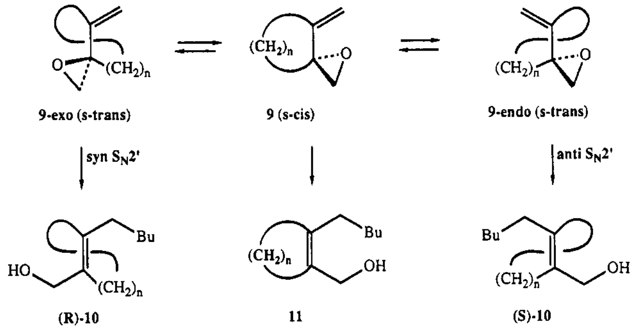


Figure 1. S_N2' additions to vinyloxiranes (**a** series, *n* = 10; **b** series, *n* = 12; **d** series, *n* = 14).

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(5) (a) Weiler, L.; Sum, F.-W. *Can J. Chem.* **1979**, *57*, 1431. (b) Marshall, J. A.; Jenson, T. M. *J. Org. Chem.* **1984**, *49*, 1707.

(6) (a) Sharpless, K. B.; Katsuki, T. *J. Am. Chem. Soc.* **1980**, *102*, 5974. (b) The reactivity order (*R*)-10 > 11 > (*S*)-10 was observed.[1d] Hence the resolved alcohols (*S*)-10 were relatively enriched in the cis isomers 11.

(7) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(8) Crandall, J. K.; Lin, L.-H. C. *J. Am. Chem. Soc.* **1967**, *89*, 4526; 4527. Kissel, C. L.; Rickborn, B. *J. Org. Chem.* **1972**, *37*, 2060.

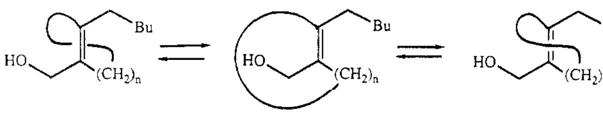
(9) Yasuda, A.; Tanaka, S.; Oshima, K.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 6513.

through analysis of the Mosher ester derivatives.[7]

Treatment of the 12-membered cycloalkylidene epoxide **9a** with the reagent *n*-butylmagnesium bromide–CuI–dimethylsulfide in THF at −20 °C afforded a 99:1 mixture of trans and cis allylic alcohols **10a** and **11a**, $[\alpha]_D$ −65.9° (corrected value −66.6°, Table I, entry 1). In an earlier study, we resolved racemic **10a** and found the *S* enantiomer of >98% optical purity to have $[\alpha]_D$ +66.4° (corrected value +67.8°, Table II, entry 1).[1a] Therefore, the foregoing addition must proceed via the syn S_N2' pathway to give the allylic alcohol (*R*)-**10a** with high stereoselectivity (Figure 1).

The 14-membered cycloalkylidene epoxide **9b** behaved analogously. Treatment with the butylcopper reagent in THF at low temperature gave a 94:6 mixture of allylic alcohols **10b** and **11b**, $[\alpha]_D$ −106.4° (corrected value −113.2°, Table I, entry 2). The sign of rotation here is suggestive of the *R* configuration, as would be expected from syn S_N2' addition to epoxide **9b** (Figure 1). This point was confirmed through Sharpless resolution of racemic **10b**[1c] using L-(+)-diisopropyl tartrate as the chiral ligand.[6] The resolved (*S*)-allylic alcohol **10b** showed $[\alpha]_D$ +132.6° (corrected value +133.3, Table II, entry 2). Thus the S_N2' addition to **9b** also proceeds with high syn stereoselectivity.

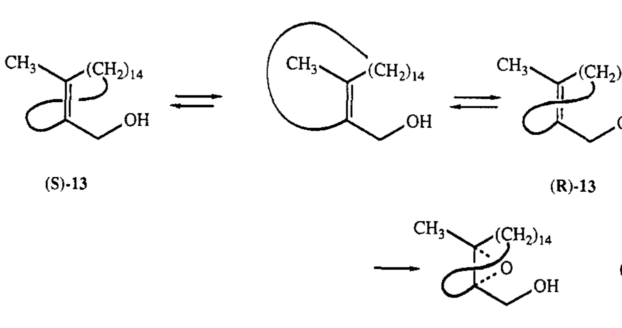
The 16-membered cycloalkylidene epoxide **9d** upon treatment with the foregoing butylcopper reagent in THF at low temperature afforded an 89:11 mixture of trans and cis allylic alcohols **10d** and **11d** of low optical rotation (Table I, entry 3). Attempted Sharpless resolution of allylic alcohol (±)-**10d** also afforded recovered allylic alcohol of low optical rotation (Table II, entry 6). We suspected that impurities were responsible for this optical activity, but attempts to purify alcohol **10d** failed to change the observed rotation. Assuming for the moment that optical activity does arise from impurities, we surmised that **10d**, unlike its smaller ring homologues, undergoes jump-rope racemization (eq 1). Presumably rotation of the methylene chain past the CH_2OH substituent is the preferred racemization pathway. Rotation in the opposite direction past the *n*-pentyl substituent would be sterically less favorable.



(R)-10 (S)-10

(1)

Interestingly, racemization of **10d** does not occur readily at −20 °C as epoxidation of racemic material with *excess* Sharpless reagent at that temperature afforded racemic trans epoxy alcohol **12d** according to Mosher ester analysis (Table II, entry 7). We have previously shown that the racemic *methyl*-substituted 16-membered cycloalkenylcarbinol (±)-**13** affords an optically active epoxide (**14**, eq 2) upon Sharpless epoxidation with excess reagent.[1d] In that case, rotation of the methylene chain past the vinylic CH_3 substituent evidently occurs rapidly relative to asymmetric epoxidation, so the more reactive enantiomer is constantly replenished. With alcohol **10d**, the increased steric size of the vinylic CH_2OH, relative to CH_3 as in **13**, prevents rotation of the methylene chain, at least at −20 °C, so the more reactive enantiomer ((*R*)-**10d**) cannot be replenished. Hence the less reactive enantiomer ((*S*)-**10d**) is eventually epoxidized as well, giving racemic epoxy alcohol **12d**. With limited Sharpless reagent, preferred epoxidation of allylic alcohol (*R*)-**10d** is observed (Table II, entry 6). However, the unreacted, optically enriched allylic alcohol (*S*)-**10d** apparently racemizes as it warms from −20 °C to room temperature during the isolation process. In contrast, both the 14- and 15-membered racemic allylic alcohols **10b** and **10c**[1c] were resolved through partial epoxidation and both gave racemic epoxy alcohols with excess Sharpless reagent (Table II, entries 2–5).

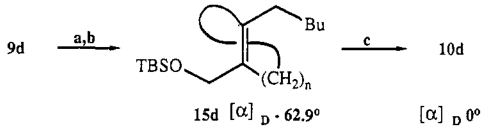


(S)-13 (R)-13

14

(2)

The formation of racemic allylic alcohol **10d** from optically active epoxide **9d** can thus be attributed to the racemization of **10d**. This racemization obviously obliterates any information on the diastereoselectivity of the S_N2' process. However, since racemization does not occur rapidly at −20 °C, we reasoned that it might be possible to trap the alkoxide intermediate from cuprate addition to **9d** at low temperature with a bulky group that would block the ring chain rotation depicted in eq 1. Indeed, when *tert*-butyldimethylsilyl chloride was added to the organocopper–epoxide reaction mixture at −20 °C, the TBS ether **15d**, $[\alpha]_D$ −62.9°, was obtained as a 93:7 cis–trans mixture (eq 3). Removal of the TBS grouping with tetra-*n*-butylammonium fluoride led to racemic alcohol **10d**.



(3)

(a) *n*-BuMgBr, CuI, Me_2S, THF, −78 to −20 °C; (b) *t*-$BuMe_2SiCl$, HMPA, −20 °C; (c) *n*-Bu_4NF, THF, −20 °C

The TBS ether **15d** obtained from this low-temperature trapping experiment compared favorably in sign and magnitude of optical rotation with the homologous TBS ether **15b** ($[\alpha]_D$ −76.7°) prepared from epoxide **9b** via the same protocol. Thus we surmise that the 16-membered cycloalkylidene epoxide **9d** also reacts with the cuprate reagent via syn S_N2' displacement, as was found for the smaller ring homologues (Figure 1).

Interestingly, purification of the allylic alcohol **10d** recovered from attempted Sharpless resolutions, as discussed above, also proved possible through the TBS ether **15d**. Cleavage of the TBS grouping from a chromatographed sample gave allylic alcohol **10d** with negligible rotation.

Although the driving force appears to be small, nearly all known reactions of organocopper reagents with vinyloxiranes proceed via anti S_N2' displacement.[4] The preferred syn addition to cycloalkylidene epoxides **9a**, **9b**, and **9d** thus runs counter to the general trend seen for conformationally fixed systems. As noted above, the two s-trans conformers of the cyclododecylidene epoxide **9a** are nearly equal in energy.[3] Ground state conformational factors are therefore an unlikely stereocontrol element. We believe that the observed selectivity may result from the differing environments of the epoxide oxygen in the two s-trans conformers. Bond breaking in the transition state of the S_N2' displacement should be facilitated by coordination of the developing alkoxide with lithium cations and solvation of the array.[1c,2] Such coordination would be blocked by the bridging methylene chain in conformer

9-endo (Figure 1), where the epoxide oxygen occupies an interannular position of the macrocycle. The syn selectivity appears to decrease with increasing ring size, although this trend could not be rigorously confirmed owing to the optical instability of the 16-membered case **10d**. Regardless, steric shielding of the epoxide oxygen would expectedly diminish with larger ring sizes, thus allowing anti S_N2' attack to occur, though perhaps not predominate until very large ring sizes are reached.

From a synthetic standpoint, the present study delineates the first route to optically active *trans*-cycloalkenes not requiring optical resolution. It also provides a third example of jump-rope racemization that occurs on a measurable time and temperature scale.[10]

Experimental Section

2-Carbethoxycyclododecanone (1a). A 2-L three-necked flask equipped with a reflux condenser and Dean–Stark trap was charged with 350 mL of benzene. Approximately 25 mL of benzene–water mixture was removed by distillation via a Dean–Stark trap followed by an additional 60 mL of dry benzene. The benzene solution was cooled to room temperature, and 11.06 g (0.461 mol) of sodium hydride was added followed by 39.98 mL (0.33 mol) of diethyl carbonate. The mixture was brought to reflux with vigorous stirring, and a solution of 30.00 g (0.165 mol) of cyclododecanone in 60 mL of benzene was added dropwise over 1.3 h to the refluxing solution. The solution was refluxed for an additional 3 h, then cooled to room temperature, and stirred overnight. The mixture was cooled to 0 °C, and 39.0 mL of acetic acid was added dropwise, followed by slow addition of 150 mL of ice water. The mixture was stirred until all solids were dissolved. The layers were separated, and acetic acid was added until the aqueous layer was weakly acidic. The aqueous layer was extracted with ether, and the combined organic layers were washed with water and brine and dried over magnesium sulfate. Acetic acid was removed by simple distillation at aspirator pressure. Kugelrohr distillation of the residue at 0.15 mm (bath temperature 116–140 °C) gave 35.5 g (84%) of a semisolid: IR (film) ν 2950, 2850, 1740, 1710, 1640, 1605, 1475, 1450, 1370, 1270, 1180, 1140 cm^{-1}; ^1H NMR (90 MHz) 1.16–1.46 (env, ring CH_2) 1.22 (t, J = 7.5 Hz, CH_3), 1.5–2.43 (m), 2.5–2.7 (m), 3.58 (dd, J = 12.0 Hz, CH), 4.13 (q, J = 7.5 Hz, OCH_2) ppm.

2-Carbethoxycyclotetradecanone (1b). To a solution of 77.0 g (0.39 mol) of cyclotridecanone in 390 mL of ether was added 52.76 mL (0.429 mol) of boron trifluoride etherate at −20 °C under nitrogen.[11] The mixture was stirred for 15 min, and then 47.49 mL (0.429 mol) of ethyl diazoacetate was added dropwise. The mixture was stirred with visible evolution of nitrogen and warmed to room temperature. After 75 h, the mixture was poured into water and extracted with ether. The combined ether layers were washed with 10% sodium hydroxide, water, and brine and dried over magnesium sulfate. Kugelrohr distillation of the residue at 0.2 mm (bath temperature 130–156 °C) gave 35.4 g (57%) of an oil: IR (film) ν 2900, 2850, 1740, 1710, 1460, 920 cm^{-1}; ^1H NMR (60 MHz) 0.92–1.52 (m, CH_3), 1.0–1.48 (env, ring CH_2), 1.58–2.2 (m), 2.38–2.98 (m), 3.35–3.68 (q, CH), 4.42 (q, J = 10.8 Hz, OCH_2) ppm. Anal. Calcd for $C_{17}H_{30}O_3$: C, 72.30; H, 10.71. Found; C, 72.17; H, 10.75.

2-Carbethoxycyclohexadecanone (1d). The procedure for **1b** was followed, with 17.24 mL (0.140 mol) of boron trifluoride etherate added to a solution of 28.60 g (0.127 mol) of cyclopentadecanone in 210 mL of ether at −20 °C under nitrogen. After 15 min, 14.72 mL (0.140 mol) of ethyl diazoacetate was added and the mixture was warmed to room temperature. After 94 h, Kugelrohr distillation at 0.3 mm (bath temperature 155–170 °C) gave 35.50 g (90%) of product: IR (film) ν 2910, 2850, 1710, 1460, 1370, 1190 cm^{-1}; ^1H NMR (90 MHz) 1.23 (t, J = 7.5 Hz, CH_3), 1.19–1.43 (env, ring CH_2), 1.43–2.03 (m), 2.56 (t, J = 7.5 Hz, CH_2CO), 3.52 (q, J = 6.0 Hz, $CHCO_2$), 4.15 (q, J = 6.8 Hz, OCH_2) ppm. Anal. Calcd for $C_{13}H_{30}O_3$: C, 73.50; H, 11.04. Found: C, 73.55; H, 11.06.

Ethyl (*Z*)-2-[(Diethoxyphosphinyl)oxy]-1-cyclotetradecenecarboxylate (2b). To a slurry of 1.866 g (0.075 mol) of 97% sodium hydride in 40 mL of ether was added 16.614 g (0.058 mol) of the β-keto ester **1b** in 20 mL of ether via syringe pump over 30 min at 0 °C under argon. The mixture was stirred for 1 h at 0 °C, heated to reflux for 3 h, and cooled to 0 °C, and 10.90 mL (0.075 mol) of diethyl chlorophosphate was added dropwise over 15 min.[5] The mixture was stirred at 0 °C for 3.5 h, then allowed to warm to room temperature, and stirred overnight. Solid ammonium chloride was carefully added at 0 °C, and the mixture was stirred for 30 min, filtered through Celite, and concentrated. The residue was taken up in ether, washed with water, saturated sodium bicarbonate, and water, and dried over magnesium sulfate. Removal of solvent gave 22.34 g (92%) of an oil: IR (film) ν 2910, 2850, 1710, 1465, 1180, 1040 cm^{-1}; ^1H NMR (90 MHz) 1.08–1.5 (env, ring CH_2), 1.53–1.80 (m), 2.13–2.60 (m), 4.0–4.4 (m) ppm.

Ethyl (*Z*)-2-[(Diethoxyphosphinyl)oxy]-1-cyclododecenecarboxylate (2a). The above procedure was followed, with 2.403 g (0.097) mol) of sodium hydride in 60 mL of ether to which was added 19.00 g (0.075 mol) of the β-keto ester **1a** in 25 mL of ether at 0 °C. The reaction mixture was stirred at 0 °C and then at reflux for 3 h, and 14.03 mL (0.097 mol) of diethyl chlorophosphate was added at 0 °C. The previously described procedure yielded 24.023 g (82%) of an oil: IR (film) ν 2910, 2850, 1710, 1460, 1190 cm^{-1}; ^1H NMR (90 MHz) 1.06–1.43 (env, ring CH_2), 1.26 (t, J = 4.5 Hz, CH_3), 1.43–1.73 (m), 2.13–2.40 (m), 4.15 (q, J = 6.0 Hz, CH_2) ppm.

Ethyl (*Z*)-2-[(Diethoxyphosphinyl)oxy]-1-cyclohexadecenecarboxylate (2d). The above procedure was followed, with 1.606 g (0.065 mol) of sodium hydride in 40 mL of ether to which was added 15.615 g (0.050 mol) of the β-keto ester **1d** in 20 mL of ether at 0 °C. The reaction mixture was stirred at 0 °C and at reflux for 3 h, and 9.46 mL (0.065 mol) of diethyl chlorophosphate was added at 0 °C. The previously described procedure yielded 17.178 g (77%) of an oil: IR (film) ν 2920, 2850, 1720, 1660, 1470, 1450, 1100, 1040, 990 cm^{-1}; ^1H NMR (90 MHz) 1.16–1.53 (env, ring CH_2), 1.31 (t, J = 6.0 Hz, CH_3), 1.56–1.86 (m), 2.16–2.60 (m), 4.18 (q, J = 7.5 Hz, OCH_2) ppm.

Ethyl (*E*)-2-Methylcyclohexadecenecarboxylate (3d). To a slurry of 19.044 g (0.100 mol) of copper iodide in 300 mL of ether was added slowly dropwise 153.8 mL (0.200 mol) of 1.3 M methyllithium complexed with lithium bromide at 0 °C under argon.[5] The mixture was stirred for 30 min, cooled to −78 °C, and stirred for 30 min, and then 22.30 g (0.050 mol) of the enol phosphate **2d** in 100 mL of ether was added. The mixture was stirred at −78 °C for 2.2 h, then quenched with 360 mL of saturated ammonium chloride, and stirred overnight. The mixture was poured into 3% ammonium hydroxide and extracted with ether. The ether layers were washed with 3% ammonium hydroxide, saturated ammonium chloride, and water and dried over magnesium sulfate. Removal of solvent and flash chromatography on silica gel (4:1 hexane–ethyl acetate) gave 13.258 g (88%) of the methyl ester as an oil: IR (film) ν 2910, 2850, 1710, 1460, 1210 cm^{-1}; ^1H NMR (90 MHz) 1.26 (t, J = 7.5 Hz, CH_3), 1.30–1.40 (env, ring CH_2), 1.85 (s, vinyl CH_3), 2.06–2.47 (m), 4.18 (q, J = 6.3 Hz, OCH_2) ppm. Anal. Calcd for $C_{20}H_{36}O_2$: C, 77.87; H, 11.86. Found: C, 78.08; H, 11.80.

Ethyl (*E*)-2-Methylcyclododecenecarboxylate (3a). The above procedure was followed, with a slurry of 17.568 g (0.092 mol) of copper iodide in 500 mL of ether to which was added over 1.5 h 133.6 mL (0.184 mol) of 1.38 M methyllithium complexed with lithium bromide at 0 °C under argon. To this mixture at −78 °C was added 24.00 g (0.062 mol) of the enol phosphate **2a** in 100 mL of ether. Workup as before gave 9.495 g (61%) of the methyl ester as an oil: IR (film) ν 2900, 2850, 1715, 1475, 1290, 1215, 1190 cm^{-1}; ^1H NMR (90 MHz) 1.28 (t, J = 7.5 Hz, CH_3), 1.30–1.73 (env, ring CH_2), 1.85 (s, vinyl CH_3), 2.06–2.47 (m), 4.18 (q, J = 7.1 Hz, OCH_2) ppm.

Ethyl (*E*)-2-Methylcyclotetradecenecarboxylate (3b). The above procedure was followed, with a slurry of 13.330 g (0.070 mol) of copper iodide in 250 mL of ether to which was added 100.0 mL of 1.4 M methyllithium complexed with lithium bromide in ether at 0 °C under argon over 1.5 h. To this mixture at −78 °C

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[10] The first example was *trans*-cyclononene. Cope, A. C.; Banholzer, K.; Keller, H.; Pawson, B. A.; Whang, J. J.; Winkler, H. J. S. *J. Am. Chem. Soc.* **1965**, *87*, 3644. The second example was *trans*-(2-methylcyclopentadecenyl)methanol (the 15-membered analogue of **13**).[1d]

[11] Marshall, J. A.; Partridge, J. J. *Tetrahedron* **1969**, *25*, 2159.

was added 14.600 g (0.035 mol) of the enol phosphate **2b** in 50 mL of ether. Workup as before gave 7.397 g (75%) of the methyl ester as an oil: IR (film) ν 2920, 2850, 1710, 1620, 1470, 1450, 1220, 920 cm^{-1}; ^{1}H NMR (90 MHz) 1.28 (t, J = 7.5 Hz, CH_3), 1.30–1.73 (env, ring CH_2), 1.85 (s, vinyl CH_3), 2.06–2.47 (m), 4.18 (q, J = 6.0 Hz, OCH_2) ppm. Anal. Calcd for $C_{18}H_{32}O_2$: C, 77.09; H, 11.50. Found: C, 76.94; H, 11.52.

(*E*)-(2-Methyl-1-cyclotetradecenyl)methanol (4b). To a solution of 4.550 g (0.016 mol) of the ester **3b** in 40 mL of hexane was added dropwise 49.0 mL (0.049 mol) of 1.0 M diisobutylaluminum hydride at −78 °C under argon. The mixture was stirred at −78 °C for 2 h, then quenched with 70 mL of saturated ammonium chloride, and warmed to room temperature. The solids were dissolved with 10% HCl, and the mixture was extracted with ether. The combined ether layers were washed with 10% HCl, water, and brine and dried over magnesium sulfate. Removal of solvent and flash chromatography on silica gel (4:1 hexane–ethyl acetate) gave 3.459 g (91%) of a white solid: mp 51.0–53.5 °C; IR (film) ν 3300, 2920, 2850, 1470, 1450, 1010 cm^{-1}; ^{1}H NMR (90 MHz) 1.23–1.56 (env, ring CH_2), 1.76 (s, vinyl CH_3), 1.93–2.30 (m), 4.15 (s, CH_2O) ppm. Anal. Calcd for $C_{16}H_{30}O$: C, 80.61; H, 12.68. Found: C, 80.70; H, 12.70.

(*E*)-(2-Methyl-1-cyclododecenyl)methanol (4a). The above procedure was followed with 9.495 g (0.038 mol) of the ester **3a** in 130 mL of hexane and 113.0 mL of 1.0 M diisobutylaluminum hydride. Following workup and flash chromatography, 6.304 g (79%) of the alcohol was obtained as a white solid: mp 40.5–42.0 °C; IR (film) ν 3300, 2900, 2845, 1470, 1440, 1000 cm^{-1}; ^{1}H NMR (90 MHz) 1.20–1.80 (env, ring CH_2), 1.77 (s, CH_3), 2.03–2.40 (m), 4.18 (s, CH_2O) ppm.

(*E*)-(2-Methyl-1-cyclohexadecenyl)methanol (4d). The above procedure was followed with 13.250 g (0.043 mol) of the ester **3d** in 108 mL of hexane and 129.0 mL of 1.0 M diisobutylaluminum hydride. Following workup and flash chromatography, 9.389 g (82%) of the alcohol was obtained as a white solid: mp 51.5–53.5 °C; IR (film) ν 3400, 2910, 2850, 1470, 1000, 920 cm^{-1}; ^{1}H NMR (90 MHz) 1.26–1.63 (env, ring CH_2), 1.72 (s, CH_3), 1.93–2.30 (m), 4.12 (s, CH_2O) ppm. Anal. Calcd for $C_{18}H_{34}O$: C, 81.13; H, 12.86. Found: C, 81.20; H, 12.87.

(1*S*,2*S*)-(2-Methyl-1,2-epoxycyclotetradecyl)methanol (5b). To a cooled solution of 80 mL of dichloromethane was added 2.76 mL (9.28 mmol) of titanium tetraisopropoxide, followed by dropwise addition of 2.07 mL (12.07 mmol) of (+)-diethyl tartrate at −23 °C under argon.[6a] The mixture was stirred for 5 min, and then 2.211 g (9.28 mmol) of the allylic alcohol **4b** in 13.0 mL of dichloromethane was added dropwise followed by 3.18 mL (11.14 mmol) of 3.5 M anhydrous *tert*-butyl hydroperoxide in 1,2-dichloroethane at −23 °C. The reaction mixture was stirred for 1.5 h at −23 °C and then stored in the freezer at −30 °C for 18.5 h. The mixture was poured into a −23 °C solution of 5.0 mL of water and 195.0 mL of acetone and stirred at −23 °C for 0.75 h and at room temperature for 2.0 h. The clear solution was filtered through Celite, concentrated, and extracted with dichloromethane. The combined extracts were dried over potassium carbonate, filtered, and concentrated under reduced pressure. Flash chromatography on silica gel (7:1 hexane–ether) afforded 1.815 g (77%) of the epoxy alcohol as a white solid: mp 62.5–65.0 °C; $[\alpha]_D$ −7.13° (*c* 3.49, $CHCl_3$); IR (film) ν 3350, 2920, 2850, 1470, 1050 cm^{-1}; ^{1}H NMR (90 MHz) 1.23–1.60 (env, ring CH_2), 1.61–2.13 (m), 2.26 (t, J = 6.0 Hz, CH_2), 3.80 (AB q, J = 3.6 Hz, $\Delta\nu$ = 5.1 Hz, CH_2O) ppm. Anal. Calcd for $C_{16}H_{30}O_2$: C, 75.54; H, 11.89. Found: C, 75.47; H, 11.94.

(1*S*,2*S*)-(2-Methyl-1,2-epoxycyclododecyl)methanol (5a). The alcohol **4a** (2.937 g, 0.014 mol) in 40 mL of dichloromethane was added to a cooled solution of 4.17 mL (0.014 mol) of titanium tetraisopropoxide and 3.12 mL (0.018 mol) of (+)-diethyl tartrate in 100 mL of dichloromethane as above. Addition of 4.80 mL (0.017 mol) of 3.5 M *tert*-butyl hydroperoxide in 1,2-dichloroethane followed by workup after 20.2 h gave upon purification 1.857 g (59%) of the epoxy alcohol as a white solid: mp 64.5–66.5 °C; $[\alpha]_D$ −9.56° (*c* 3.83, $CHCl_3$); IR (film) ν 3400, 3000, 2900, 2850, 1480, 1450, 1390, 1220, 1020 cm^{-1}; ^{1}H NMR (90 MHz) 1.17–1.70 (env, ring CH_2), 1.84 (s, CH_3), 3.78 (AB q, J = 11.7 Hz, $\Delta\nu$ = 13.7 Hz, CH_2O) ppm.

(1*S*,2*S*)-(2-Methyl-1,2-epoxycyclohexadecyl)methanol (5d). The alcohol **4d** (1.036 g, 3.89 mmol) in 18 mL of dichloromethane was added to a cooled solution of 1.16 mL (3.89 mmol) of titanium tetraisopropoxide and 0.87 mL (5.06 mmol) of (+)-diethyl tartrate in 22 mL of dichloromethane as above. Addition of 1.33 mL of 3.5 M *tert*-butyl hydroperoxide in 1,2-dichloroethane followed by workup after 16.5 h gave upon purification 0.808 g (74%) of the epoxy alcohol as a white solid: mp 44.5–46.0 °C; $[\alpha]_D$ −5.82° (*c* 3.57, $CHCl_3$); IR (film) ν 3400, 2910, 2850, 1470, 1050 cm^{-1}; ^{1}H NMR (90 MHz) 1.23–1.63 (env, ring CH_2), 1.73–2.23 (m), 3.73 (br s, CH_2O) ppm. Anal. Calcd for $C_{18}H_{34}O_2$: C, 76.54; H, 12.13. Found: C, 76.54; H, 12.14.

(−)-2-Methylene-1-(hydroxymethyl)cyclotetradecan-1-ol (6b). The procedure of Williams was modified.[9,12] To a solution of 0.66 mL (3.9 mmol) of 2,2,6,6-tetramethylpiperidine in 4.0 mL of benzene was added 1.50 mL (3.9 mmol) of 2.6 M *n*-butyllithium in hexane at 0 °C under argon. The mixture was stirred at 0–3 °C for 30 min, and then 4.11 mL (3.9 mmol) of 0.95 M diethylaluminum chloride was added dropwise. The white mixture was stirred at 0–3 °C for 40 min, and then 0.248 g (0.97 mmol) of the epoxy alcohol **5b** in 2.1 mL of benzene was added. The mixture was stirred for 5 h at 0 °C, then quenched with saturated ammonium chloride, warmed to room temperature, filtered through Celite, and concentrated. The residue was taken up in ether, poured into water, extracted with ether, washed with water, and dried over potassium carbonate. Removal of solvent and flash chromatography on silica gel (20:1 hexane–ethyl acetate) afforded 0.159 g (64%) of a solid: mp 79.5–80 °C; $[\alpha]^{24}_D$ −14.44° (*c* 3.4, $CHCl_3$); IR (film) ν 3400, 2920, 2850, 1640, 1460, 1060, 910 cm^{-1}; ^{1}H NMR (90 MHz) 1.0–1.70 (env, ring CH_2), 1.76–2.0 (m), 2.18–2.60 (m), 3.52 (AB q, J = 11.7 Hz, $\Delta\nu$ = 17.05 Hz, CH_2O), 5.03, 5.52 (s, $CH_2{=}C$) ppm. Anal. Calcd for $C_{16}H_{30}O_2$: C, 75.53; H, 11.89. Found: C, 75.44; H, 11.96.

(+)-2-Methylene-1-(hydroxymethyl)cyclododecan-1-ol (6a). The above procedure was followed, with a solution of 0.40 mL (2.36 mmol) of 2,2,6,6-tetramethylpiperidine in 1.70 mL of benzene to which 0.91 mL (2.36 mmol) of 2.6 M *n*-butyllithium in hexane was added. After 25 min, 2.36 mL (2.36 mmol) of 1.0 M diethylaluminum chloride was added. The mixture was stirred for 40 min, and then 0.150 g (0.66 mmol) of the epoxy alcohol **5a** in 2.3 mL of benzene was added. Following workup and flash chromatography, 0.077 g (51%) of a solid was obtained: mp 73.5–75.0 °C; $[\alpha]^{23}_D$ +26.3° (*c* 1.9, $CHCl_3$); IR (film) ν 3400, 2900, 2850, 1640, 1470, 1040, 910 cm^{-1}; ^{1}H NMR (90 MHz) 1.08–1.60 (env, ring CH_2), 1.90–2.10 (m), 2.26–2.40 (m), 3.48 (AB q, J = 11.25 Hz, $\Delta\nu$ = 21.0 Hz, CH_2O), 5.03, 5.23 (s, $CH_2{=}C$) ppm. Anal. Calcd for $C_{14}H_{26}O_2$: C, 74.29; H, 11.58. Found: C, 74.20; H, 11.61.

(−)-2-Methylene-1-(hydroxymethyl)cyclohexadecan-1-ol (6d). The above procedure was followed, with a solution of 0.45 mL (2.69 mmol) of 2,2,6,6-tetramethylpiperidine in 2.0 mL of benzene to which 1.22 mL (2.69 mmol) of 2.2 M *n*-butyllithium in hexane was added. After 40 min, 2.83 mL (2.69 mmol) of 0.95 M diethylaluminum chloride was added. The mixture was stirred for 35 min, and then 0.190 g (0.67 mmol) of the epoxy alcohol **5d** in 2.2 mL of benzene was added. Following workup and flash chromatography, 0.100 g (53%) of a solid was obtained: mp 70.5–73.0 °C; $[\alpha]^{26}_D$ −5.12° (*c* 4.1, $CHCl_3$); IR (film) ν 3425, 2950, 2810, 1645, 1470, 1220, 1180, 920 cm^{-1}; ^{1}H NMR 1.10–1.66 (env, ring CH_2), 1.73–2.05 (m), 2.37–2.62 (m), 3.48 (AB q, J = 9.9 Hz, $\Delta\nu$ = 15.6 Hz, CH_2O), 5.03, 5.16 (s, $CH_2{=}C$) ppm. Anal. Calcd for $C_{18}H_{34}O_2$: C, 76.54; H, 12.13. Found: C, 76.63; H, 12.12.

(2-Methylene-1-hydroxy-1-cyclododecyl)methyl *p*-Toluenesulfonate (8a). To a solution of 0.066 g (0.29 mmol) of the diol **6a** in 1.0 mL of dichloromethane was added 0.05 mL (0.35 mmol) of triethylamine followed by 0.015 g (0.12 mmol) of 4-(*N*,*N*-dimethylamino)pyridine and 0.061 g (0.32 mmol) of *p*-toluenesulfonyl chloride at 0 °C under argon. The mixture was stirred overnight at 0 °C, then poured into water, and extracted with dichloromethane. The combined dichloromethane layers were washed with water, saturated copper sulfate, and water and dried over magnesium sulfate. Removal of solvent afforded 0.093 g (85%) of a light yellow solid: IR (film) ν 3500, 2920, 2850, 1640, 1600, 1470, 1360, 1200, 1180, 980 cm^{-1}; ^{1}H NMR (90 MHz) 1.07–1.80 (env, ring CH_2), 1.81–2.13 (m), 2.27 (s), 2.45 (s, CH_3), 3.00 (s), 4.00 (AB q, J = 10.8 Hz, $\Delta\nu$ = 11.5 Hz, CH_2O), 5.05, 5.26

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(12) Williams, D. R.; Sit, S.-Y. *J. Am. Chem. Soc.* **1984**, *106*, 2949.

(s, CH_2=C), 7.58 (AB q, J = 9.0 Hz, $\Delta\nu$ = 39.5 Hz, aryl H's) ppm.

(2-Methylene-1-hydroxy-1-cyclotetradecyl)methyl *p*-Toluenesulfonate (8b). The above procedure was followed, with a solution of 0.071 g (0.28 mmol) of the diol **6b** in 0.85 mL of dichloromethane to which was added 0.05 mL (0.33 mmol) of triethylamine, 0.017 g (0.14 mmol) of 4-(*N*,*N*-dimethylamino)pyridine, and 0.059 g (0.31 mmol) of *p*-toluenesulfonyl chloride. Following workup, 0.101 g (88%) of the solid tosylate was obtained: IR (film) ν 3500, 2920, 2850, 1640, 1605, 1370, 1200, 1190 cm^{-1}; ^{1}H NMR (90 MHz), 1.0–1.73 (env, ring CH_2), 2.73 (s), 2.95 (s, CH_3), 3.95 (s, CH_2O), 4.98, 5.20 (s, CH_2=C), 7.56 (AB q, J = 8.4 Hz, $\Delta\nu$ = 41.0 Hz, aryl H's) ppm.

(2-Methylene-1-hydroxy-1-cyclohexadecyl)methyl *p*-Toluenesulfonate (8d). The above procedure was followed, with a solution of 0.143 g (0.50 mmol) of the diol **6d** in 1.3 mL of dichloromethane to which was added 0.09 mL (0.61 mmol) of triethylamine, 0.032 g (0.26 mmol) of 4-(*N*,*N*-dimethylamino)pyridine, and 0.107 g (0.56 mmol) of *p*-toluenesulfonyl chloride. Following workup, 0.186 g (85%) of the tosylate was obtained as a solid: IR (film) ν 3500, 2910, 2845, 1600, 1475, 1190, 1180, 970 cm^{-1}; ^{1}H NMR (90 MHz) 1.03–1.60 (env, ring CH_2), 1.63–1.93 (m), 2.43 (s, CH_3), 3.98 (s, CH_2O), 4.98, 5.12 (s, CH_2=C), 7.56 (AB q, J = 9.0 Hz, $\Delta\nu$ = 37.6 Hz, aryl H's) ppm.

(−)-4-Methylene-1-oxaspiro[2.11]tetradecane (9a). To a solution of 0.150 g (0.39 mmol) of the tosylate **8a** in 2.0 mL of ether was added dropwise 0.27 mL (0.59 mmol) of benzyltrimethylammonium hydroxide as a 40 wt % solution in methanol at room temperature under argon.[13] The mixture was stirred for 2 h, then poured into water, and extracted with ether. The combined ether layers were washed with water and dried over potassium carbonate. Removal of solvent and flash chromatography on silica gel (deactivated with 4% triethylamine–hexane) with hexane eluant gave 0.050 g (62%) of the epoxide as an oil: $[\alpha]^{23}_D$ −46.1° (*c* 5.0, $CHCl_3$); IR (film) ν 2900, 2845, 1630, 1475, 1450, 900 cm^{-1}; ^{1}H NMR (90 MHz) 1.23–1.90 (env, ring CH_2), 1.91–2.30 (m), 2.65, (s, OCH_2), 5.02, 5.16 (C=CH_2) ppm; GC/MS, *m*/*e* (M^+) 208, calcd (M^+) 208.3.

(−)-4-Methylene-1-oxaspiro[2.13]hexadecane (9b). The above procedure was modified. To 0.217 g (0.53 mmol) of the tosylate **8b** in 2.3 mL of ether was added 0.37 mL (0.80 mmol) of benzyltrimethylammonium hydroxide as a 40 wt % solution in methanol at room temperature under argon. The mixture was stirred for 3 h, and then workup and purification as before gave 0.091 g (72%) of the epoxide as an oil: $[\alpha]^{25}_D$ −63.4° (*c* 5.8, $CHCl_3$); IR (film) ν 2900, 2845, 1630, 1475, 1450, 900 cm^{-1}; ^{1}H NMR (90 MHz) 1.20–1.70 (env, ring CH_2), 1.80–2.17 (m), 2.65 (AB q, J = 5.4 Hz, $\Delta\nu$ = 8.3 Hz, CH_2O), 4.9, 5.1 (s, CH_2=C) ppm; GC/MS, *m*/*e* (M^+) 236, calcd (M^+) 236.4.

(−)-4-Methylene-1-oxaspiro[2.15]octadecane (9d). The above procedure was followed, with a solution of 0.180 g (0.41 mmol) of the tosylate **8d** in 1.5 mL of ether to which was added 0.29 mL (0.62 mmol) of benzyltrimethylammonium hydroxide as a 40 wt % solution in methanol at room temperature under argon. Workup and purification afforded 0.077 g (71%) of the epoxide as an oil: $[\alpha]^{23}_D$ −54.9° (*c* 5.30, $CHCl_3$); IR (film) ν 2910, 2850, 1640, 1470, 920 cm^{-1}; ^{1}H NMR (90 MHz) 1.20–1.63 (env, ring CH_2), 1.83–2.20 (m), 2.62 (AB q, J = 5.4 Hz, $\Delta\nu$ = 10.3 Hz, CH_2O), 4.88, 5.07 (s, CH_2=C) ppm; GC/MS, *m*/*e* (M^+) 264, calcd (M^+) 264.5.

Cuprate Additions. (±)-(*Z*)-(2-Pentyl-1-cyclohexadecenyl)methanol (10d). The procedure of Marshall and Flynn was followed.[1a] To a slurry of 0.101 g (0.53 mmol) of copper iodide in 1.5 mL of tetrahydrofuran was added 0.23 mL (3.18 mmol) of dimethyl sulfide under argon. The solution was cooled to −78 °C, and 1.06 mL (0.53 mmol) of 0.50 M *n*-butylmagnesium bromide was added dropwise. The orange mixture was stirred for 15 min, and then 0.070 g (0.26 mmol) of the epoxide **9d** in 2.0 mL of tetrahydrofuran was added dropwise. The mixture was allowed to warm slowly from −78 to −20 °C overnight, and then it was diluted with saturated ammonium chloride, stirred for 1 h at room temperature, poured into 3% ammonium hydroxide, and extracted with ether. The combined ether layers were washed with 3% ammonium hydroxide, water, and saturated ammonium chloride and dried over potassium carbonate. Removal of solvent and flash chromatography on silica gel (7:1 hexane–ether) gave 0.055 g (66%) of the allylic alcohol as an 89:11 mixture of trans and cis isomers: $[\alpha]^{25}_D$ −0.4° (*c* 2.38, $CHCl_3$); IR (film) ν 3350, 2910, 2850, 1470, 1000 cm^{-1}; ^{1}H NMR (90 MHz) 0.88 (t, J = 7.5 Hz, CH_3CH_2), 1.0–1.6 (env, ring CH_2), 1.73–2.62 (m), 4.13 (AB q, J = 10.8 Hz, $\Delta\nu$ = 39.0 Hz, CH_2OH, trans), 4.12 (s, CH_2OH, cis) ppm. Anal. Calcd for $C_{22}H_{42}O$: C, 81.92; H, 13.12. Found: C, 81.67; H, 13.15. The Mosher ester derivative exhibited resonances at 4.659 and 4.609 ppm in the ^{19}F NMR spectrum in the ratio 50:50.[7]

(−)-(*Z*)-(2-Pentyl-1-cyclododecenyl)methanol (10a). The above procedure was followed. Addition of 0.026 g (0.12 mmol) of the epoxide **9a** to the cuprate complex at −78 °C and stirring at −78 to −20 °C followed by workup and flash chromatography on silica gel (5:1 hexane–ether) afforded 0.021 g (68%) of the alcohol as a white solid: mp 59.5–61.5 °C; $[\alpha]^{25}_D$ −65.9° (*c* 2.0, $CHCl_3$); IR (film) ν 3400, 2900, 2850, 1640, 1475, 1010 cm^{-1}; ^{1}H NMR (90 MHz) 0.8–0.98 (m, CH_3CH_2), 1.0–1.66 (env, ring CH_2), 1.8–2.23 (m), 2.26–2.66 (m), 4.25 (AB q, J = 10.5 Hz, $\Delta\nu$ = 50.2 Hz, trans CH_2O). Anal. Calcd for $C_{18}H_{34}O$: C, 81.13; H, 12.86. Found: C, 81.19; H, 12.89. The Mosher ester derivative exhibited resonances at 4.630 and 4.519 ppm in the ^{19}F NMR spectrum in the ratio 96:4.[7]

(−)-(*Z*)-(2-Pentyl-1-cyclotetradecenyl)methanol (10b). The above procedure was followed. Addition of 0.088 g (0.37 mmol) of the epoxide **9b** to the cuprate complex at −78 °C and stirring at −78 to −20 °C followed by workup and flash chromatography on silica gel (7:1 hexane–ether) afforded 0.070 g (65%) of the alcohol as a 94:6 mixture of trans and cis isomers: $[\alpha]^{25}_D$ −93.2° (*c* 0.88, $CHCl_3$); IR (film) ν 3400, 2910, 2850, 1460, 1000 cm^{-1}; ^{1}H NMR (90 MHz) 0.78–0.90 (m, CH_3CH_2), 1.0–1.6 (env, ring CH_2), 1.67–2.63 (m), 4.15 (AB q, J = 10.8 Hz, $\Delta\nu$ = 41.4 Hz, trans CH_2OH), 4.12 (s, cis CH_2OH) ppm. Anal. Calcd for $C_{20}H_{38}O$: C, 81.56; H, 13.00. Found: C, 81.51; H, 13.07. The Mosher ester derivative exhibited resonances at 4.666 and 4.591 ppm in the ^{19}F NMR spectrum in the ratio 91:9.[7]

Sharpless Resolutions. (+)-(*S*)-(*Z*)-(2-Pentyl-1-cyclopentadecenyl)methanol ((*S*)-10c). The procedure of Sharpless and Katsuki was followed.[6a] To a cooled solution of 3.0 mL of dichloromethane was added dropwise 0.16 mL (0.55 mmol) of titanium tetraisopropoxide followed by 0.13 mL (0.63 mmol) of (+)-diisopropyl tartrate at −23 °C under argon. The mixture was stirred for 5 min, and then 0.162 g (0.52 mmol) of a 93:7 mixture of the allylic alcohols (±)-**10c** and **11c** in 2.8 mL of dichloromethane was added followed by 0.091 mL (0.32 mmol) of 3.5 M anhydrous *tert*-butyl hydroperoxide in dichloroethane. After 12 min, the mixture was diluted with 4.0 mL of acetone and 0.5 mL of water. After the mixture was stirred for 1.5 h at −23 °C and for 2.5 h at room temperature, it was filtered through a pad of Celite, concentrated, and extracted with dichloromethane. The combined extracts were washed with water, dried over K_2CO_3, filtered, and concentrated under reduced pressure. Flash chromatography of the residue on silica gel (7:1 hexane–ether) afforded 0.067 g (41%) of a 91:9 trans–cis mixture of (*S*)-**10c** and **11c**: $[\alpha]^{24}_D$ +110.3° (*c* 6.7, $CHCl_3$); IR (film) ν 3300, 2900, 2850, 1470, 1385, 1010 cm^{-1}; ^{1}H NMR (90 MHz) 0.80–1.03 (m, CH_3CH_2), 1.06–1.63 (env, ring CH_2), 1.70–2.66 (m), 4.13 (AB q, J = 11.7 Hz, $\Delta\nu$ = 44.4 Hz, trans CH_2O), 4.10 (s, cis CH_2O) ppm. Calcd for $C_{21}H_{40}O$: C, 81.75; H, 13.07. Found: C, 81.61; H, 13.12.

The Anderson–Shapiro cyclic phosphate ester derivative exhibited a resonance at −126.18 ppm in the ^{31}P NMR spectrum.[14] The corresponding spectrum of the cyclic phosphate derivative of the racemic alcohol mixture contained two peaks in the ratio 51:49 at −126.144 and −126.184 ppm.

Continued elution of the above column gave 0.070 g (41%) of the epoxy alcohol (*S*,*R*)-**12c**: $[\alpha]^{24}_D$ −58.4° (*c* 6.96, $CHCl_3$); IR (film) ν 3420, 2910, 2850, 1470, 1050 cm^{-1}; ^{1}H NMR (90 MHz) 0.80–1.03 (m, CH_3CH_2), 1.10–1.60 (env, ring CH_2), 3.75 (AB q, J = 11.7 Hz, $\Delta\nu$ = 21.3 Hz, CH_2OH) ppm. Anal. Calcd for $C_{21}H_{40}O_2$: C, 77.72; H, 12.42. Found: C, 77.86; H, 12.44.

The cyclic phosphate derivative exhibited resonances at −126.18 and −126.14 ppm in the ratio 84:16 in the ^{31}P spectrum.[14] The corresponding spectrum of the cyclic phosphate derivative of the

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racemic alcohol mixture contained two peaks in the ratio 51:49 at −126.19 and −126.14 ppm.

(+)-(*S*)-(*Z*)-(2-Pentyl-1-cyclododecenyl)methanol ((*S*)-10a). The procedure described above for (*S*)-**10c** was followed. Addition of 0.376 g (1.41 mmol) of a 98:2 mixture of the alcohols (±)-**10a** and **11a** in 4.0 mL of dichloromethane to a cooled solution of 0.44 mL (1.48 mmol) of titanium tetraisopropoxide and 0.36 mL (1.70 mmol) of (+)-diisopropyl tartrate in 14.0 mL of dichloromethane at −23 °C was followed by addition of 0.18 mL (0.85 mmol) of 4.68 M anhydrous *tert*-butyl hydroperoxide in dichloroethane. After 42 min, the product was isolated as above. Flash chromatography on silica gel (10:1 hexane–ethyl acetate) gave 0.131 g (35%) of a 98:2 mixture of alcohols (*S*)-**10a** and **11a**: $[\alpha]^{25}_{D}$ +66.5° (c 4.97, $CDCl_3$); IR (film) ν 3350, 2910, 2850, 1470, 1000 cm^{-1}; ^1H NMR (90 MHz) 0.76–1.03 (m, CH_3CH_2), 1.06–1.66 (env, ring CH_2), 1.73–2.68 (m), 4.18 (AB q, J = 11.7 Hz, $\Delta\nu$ = 49.93 Hz, trans CH_2O) ppm. Anal. Calcd for $C_{18}H_{34}O$: C, 81.13; H, 12.86. Found: C, 81.39; H, 12.97. The Mosher ester derivatie exhibited resonances at 4.37 and 4.28 ppm in the ratio 98:2 in the ^{19}F spectrum.[7] The Mosher derivative of the racemic alcohol gave resonances at 4.39 and 4.30 ppm in the ratio 51:49.

Continued elution of the above column gave 0.231 g (58%) of the epoxy alcohol **12a**: $[\alpha]^{25}_{D}$ −50.2 (c 4.84, $CDCl_3$); IR (film) ν 3410, 2920, 2850, 1470, 1040 cm^{-1}; ^1H NMR (90 MHz) 0.76–1.0 (m, CH_3CH_2), 1.05–1.68 (env, ring CH_2), 1.73–2.36 (m), 2.54 (s, OH), 3 75 (AB q, J = 10.8 Hz, $\Delta\nu$ = 28.6 Hz, CH_2O) ppm. Anal. Calcd for $C_{18}H_{34}O_2$: C, 76.54; H, 12.13. Found: C, 76.39; H, 12.08.

The Mosher ester derivative of the epoxy alcohol exhibited resonances at 3.57 and 3.53 ppm in the ratio 78:22 in the 300-MHz ^1H spectrum. The Mosher derivative of the racemic epoxy alcohol exhibited peaks at 3.57 and 3.53 ppm in the ratio 50:50.[7]

(+)-(*S*)-(*Z*)-(2-Pentyl-1-cyclotetradecenyl)methanol ((*S*)-10b). The procedure described above for (*S*)-**10a** was followed. Addition of 0.233 g (0.79 mmol) of an 80:20 mixture of the allylic alcohols (±)-**10b** and **11b** in 2.0 mL of dichloromethane to a cooled solution of 0.26 mL (0.87 mmol) of titanium tetraisopropoxide and 0.22 mL (1.03 mmol) of (+)-diisopropyl tartrate in 6.0 mL of dichloromethane at −23 °C was followed by addition of 0.14 mL (0.47 mmol) of 3.4 M anhydrous *tert*-butyl hydroperoxide in dichloroethane. After 20 min, the product was isolated as above. Flash chromatography on silica gel (10:1 hexane–ethyl acetate) afforded 0.094 g (40%) of a 72:28 mixture of alcohols **10b** and **11b**; $[\alpha]^{22}_{D}$ +96.0° (c 2.32, $CHCl_3$); IR (film) ν 3300, 2910, 2850, 1470, 1000 cm^{-1}; ^1H NMR (300 MHz) 0.84–0.93 (m, CH_3CH_2), 1.03–1.73 (env, ring CH_2), 1.95–2.45 (m), 4.11 (AB q, J = 11.6 Hz, $\Delta\nu$ = 141.8 Hz, trans CH_2O), 4.10 (s, cis CH_2O) ppm. Anal. Calcd for $C_{20}H_{38}O$: C, 81.56; H, 13.00. Found: C, 81.42; H, 13.00.

The Mosher ester derivative exhibited resonances at 4.403, 4.456, and 4.507 ppm in the ^{19}F spectrum in the ratio 76.3:0.6:23.1.[7] The corresponding spectrum for the racemic derivative contained three peaks in the ratio 37.6:39.8:22.6 at 4.373, 4.449, and 4.474 ppm. The peak at 4.474 is the cis isomer.

Continued elution of the above column gave 0.0760 g (31%) of the epoxy alcohol (*S*,*R*)-**12b**: $[\alpha]^{23}_{D}$ −66.2° (c 2.90, $CHCl_3$); IR (film) ν 3400, 2900, 2840, 1470, 1050 cm^{-1}; ^1H NMR (300 MHz) 0.83–1.01 (m, CH_3CH_2), 1.05–1.42 (env, ring CH_2), 1.43–1.77 (m), 1.88–2.02 (m), 2.07–2.20 (m), 2.23–2.25 (m), 3.77 (AB q, J = 11.7 Hz, $\Delta\nu$ = 56.3 Hz, CH_2O) ppm. Anal. Calcd for $C_{20}H_{38}O_2$: C, 77.36; H, 12.33. Found: C, 77.18; H, 12.29.

The Mosher ester derivative exhibited resonances at 3.56 and 3.53 ppm in the 300-MHz ^1H spectrum in the ratio 89:11.[7] The corresponding ^1H spectrum of the Mosher derivative of the racemic epoxy alcohol exhibited resonances at 3.56 and 3.53 ppm in the ratio 51:49.

(*Z*)-(2-Pentyl-1-cyclohexadecenyl)methanol (10d). The procedure described above for (*S*)-**10c** was followed. Addition of 0.065 g (0.20 mmol) of a 90:10 mixture of the alcohols (±)-**10d** and **11d** in 1.25 mL of dichloromethane to a cooled solution of 0.07 mL (0.22 mmol) of titanium tetraisopropoxide and 0.06 mL (0.26 mmol) of (+)-diisopropyl tartrate in 0.75 mL of dichloromethane at −23 °C was followed by addition of 0.035 mL (0.12 mmol) of 3.4 M anhydrous *tert*-butyl hydroperoxide in dichloroethane. After 16 min, the product was isolated as above. Flash chromatography on silica gel (10:1 hexane–ethyl acetate) gave 0.021 g (33%) of the alcohol **10d**: $[\alpha]^{23}_{D}$ +0.7° (c 2.1, $CHCl_3$); IR (film) ν 3300, 2910, 2845, 1465, 1000 cm^{-1}; ^1H NMR (90 MHz) 0.76–1.0 (m, CH_3CH_2), 1.01–1.53 (env, ring CH_2), 1.54–2.56 (m), 4.12 (AB q, J = 12.2 Hz, $\Delta\nu$ = 37.2 Hz, trans CH_2O), 4.10 (s, cis CH_2O) ppm. Anal. Calcd for $C_{21}H_{40}O$: C, 81.75; H, 13.07. Found: C, 81.61; H, 13.12.

Continued elution of the above column gave 0.019 g (29%) of the epoxy alcohol (*S*,*R*)-**12d**: $[\alpha]^{23}_{D}$ −36.3° (c 1.9, $CHCl_3$); IR (film) ν 3400, 2910, 2840, 1465, 1050 cm^{-1}; ^1H NMR (90 MHz) 0.76–1.0 (m, CH_3CH_2), 1.06–1.63 (env, ring CH_2), 1.66–2.25 (m), 3.5–3.98 (m) ppm. Anal. Calcd for $C_{22}H_{42}O_2$: C, 77.72; H, 12.42. Found: C, 77.86; H, 12.44.

The Anderson–Shapiro derivative of a sample of epoxy alcohol **12d** with measured $[\alpha]^{24}_{D}$ −37.5° (c 4.20, $CHCl_3$) indicated a 92:8 ratio of diastereomers.[14]

Sharpless Epoxidations. (±)-(2-Pentyl-1,2-epoxycyclohexadecyl)methanol (12d). The procedure of Sharpless and Katsuki was followed.[6a] To a cooled solution of 8.0 mL of dichloromethane was added dropwise 1.11 mL (3.74 mmol) of titanium tetraisopropoxide followed by 0.91 mL (4.32 mmol) of (±)-diisopropyl tartrate at −23 °C under argon. The mixture was stirred for 5 min, and 0.466 g (1.44 mmol) of the allylic alcohol **10d** (93:7 trans–cis mixture) in 6.0 mL of dichloromethane was added followed by 0.63 mL (2.16 mmol) of 3.45 M anhydrous *tert*-butyl hydroperoxide in dichloroethane. After 3.5 h, the mixture was diluted with a cold solution of 30.0 mL of acetone and 3.0 mL of water. After the mixture was stirred for 0.5 h at −23 °C and for 3 h at room temperature, it was filtered through a pad of Celite, concentrated, and extracted with dichloromethane. The combined extracts were washed with water, dried over K_2CO_3, filtered, and concentrated under reduced pressure. Flash chromatography of the residue on silica gel (10:1 hexane–ethyl acetate) afforded 0.302 g (62%) of the epoxy alcohol **12d**: $[\alpha]^{24}_{D}$ −1.50° (c 6.00, $CHCl_3$); IR (film) ν 3400, 2900, 2845, 1460, 1050 cm^{-1}; ^1H NMR (90 MH) 0.75–1.05 (m, CH_3CH_2), 1.06–1.63 (env, ring CH_2), 1.63–2.32 (m), 3.75 (AB q, J = 11.25 Hz, $\Delta\nu$ = 19.49 Hz, upon addition of D_2O, CH_2OH) ppm. Anal. Calcd for $C_{22}H_{42}O_2$: C, 78.04; H, 12.50. Found: C, 78.13; H, 12.51.

The Mosher ester derivative, prepared according to Sharpless and Katsuki,[6a] exhibited resonances at 3.57 and 3.53 ppm for the methoxy groups of the trans diastereoisomers in the ratio 52:48. The corresponding spectrum of the Mosher ester derived from the racemic alcohol contained two peaks in the ratio 50:50 at these positions.

(±)-(2-Pentyl-1,2-epoxycyclotetradecyl)methanol (12b). As described above, a solution of 0.121 g (0.41 mmol) of a 92:8 mixture of racemic **10b** and **11b** in 2.5 mL of dichloromethane was added to a cooled solution of 0.32 mL (1.07 mmol) of titanium tetraisopropoxide and 0.26 g (1.23 mmol) of (+)-diisopropyl tartrate in 2.0 mL of dichloromethane. Addition of 0.18 mL (0.62 mmol) of 3.4 M anhydrous *tert*-butyl hydroperoxide in dichloroethane followed by workup after 6.8 h gave upon purification 0.078 g (62%) of the epoxy alcohol **12b**: $[\alpha]^{22}_{D}$ −1.04° (c 2.1, $CHCl_3$); IR (film) ν 3400, 2900, 2845, 1460, 1220, 1040 cm^{-1}; ^1H NMR (90 MHz) 0.76–1.05 (m, CH_3CH), 1.03–1.68 (env, ring CH_2), 1.68–2.33 (m), 3.75 (AB q, J = 7.5 Hz, $\Delta\nu$ = 10.67 Hz, CH_2OH) ppm. Anal. Calcd for $C_{20}H_{38}O_2$: C, 77.36; H, 12.33. Found: C, 77.18; H, 12.29.

(±)-(2-Pentyl-1,2-epoxycyclopentadecyl)methanol (12c). As described above, a solution of 0.092 g (0.298 mmol) of a 98:2 mixture of racemic **10c** and **11c** in 1.5 mL of dichloromethane was added to a cooled solution of 0.23 mL (0.78 mmol) of titanium tetraisopropoxide and 0.19 mL (0.89 mmol) of (+)-diisopropyl tartrate in 2.0 mL of dichloromethane. Addition of 0.13 mL (0.45 mmol) of 3.4 M anhydrous *tert*-butyl hydroperoxide in dichloroethane followed by workup after 5 h gave upon purification 0.053 g (55%) of the epoxy alcohol **12c**: $[\alpha]^{23}_{D}$ −0.10° (c 1.1, $CHCl_3$); IR (film) ν 3410, 2920, 2850, 1475, 1050 cm^{-1}; ^1H NMR (90 MHz) 0.76–1.03 (m, CH_3CH_2), 1.06–1.58 (env, ring CH_2), 1.63–2.23 (m), 3.38–3.98 (m, CH_2OH) ppm. Anal. Calcd for $C_{21}H_{40}O_2$: C, 77.72; H, 12.42. Found: C, 77.86; H, 12.44.

Silyl Ether Trapping Experiments. (*R*)-(−)-2-Pentyl-1-((*tert*-butyldimethylsiloxy)methyl)cyclotetradecene (15b). To 0.093 g (0.49 mmol) of copper iodide in 2.0 mL of tetrahydrofuran was added 0.22 mL (2.9 mmol) of dimethyl sulfide under argon. The solution was cooled to −78 °C, and 0.98 mL (0.49 mmol) of 0.5 M *n*-butylmagnesium bromide was added dropwise. The orange mixture was stirred for 25 min, then 0.058

g (0.25 mmol) of the epoxide **9b** in 1.0 mL of tetrahydrofuran was added, and the mixture was stirred with warming from −78 to −20 °C overnight. To the deep purple mixture was added 0.32 mL (1.88 mmol) of hexamethylphosphoric triamide at −20 °C. After 30 min, 0.031 g (0.25 mmol) of 4-(*N*,*N*-dimethylamino)pyridine and 0.191 g (1.20 mmol) of *tert*-butyldimethylsilyl chloride in 1.0 mL of tetrahydrofuran were added and the mixture was stirred for 4 h at −20 °C, then diluted with water, and extracted with ether. The combined ether layers were washed with water, dried over K_2CO_3, and concentrated. Flash chromatography on basic alumina (I) with hexane afforded 0.047 g (46%) of the ether, a 93:7 trans–cis mixture, as an oil: $[\alpha]^{23}{}_D$ −76.7° (*c* 2.58, $CHCl_3$); IR (film) ν 2900, 2840, 1465, 1260, 1080 cm^{-1}; ^1H NMR (90 MHz) 0.02 (s, CH_3Si), 0.86 (s, $(CH_3)_3C$), 0.95–1.55 (env, ring CH_2), 1.60–2.43 (m), 4.16 (AB q, $J = 12.6$ Hz, $\Delta\nu = 30.3$ Hz, trans CH_2O), 4.05 (s, cis CH_2O) ppm. Anal. Calcd for $C_{26}H_{52}OSi$: C, 76.39; H, 12.82. Found: C, 76.45; H, 12.86. Integration of the ^1H NMR spectrum indicated a 93:7 mixture of trans–cis isomers.

(*R*)-(−)-2-Pentyl-1-((*tert*-butyldimethylsiloxy)methyl)cyclohexadecene (15d). The procedure described above for **15b** was followed. Addition of 0.092 g (0.35 mmol) of the epoxide **9d** in 1.0 mL of tetrahydrofuran to the cuprate complex at −78 °C and stirring for 18 h at −78 to −20 °C followed by addition of 0.48 mL (2.75 mmol) of hexamethylphosphoric triamide, 0.043 g (0.35 mmol) of (dimethylamino)pyridine, and 0.272 g (1.80 mmol) of *tert*-butyldimethylsilyl chloride with stirring for 20 h gave upon workup and chromatography 0.072 g (48%) of the ether, a 93:7 trans–cis mixture, as an oil: $[\alpha]_D$ −62.9° (*c* 3.34, $CHCl_3$); IR (film) ν 2900, 2840, 1465, 1260, 1080 cm^{-1}; ^1H NMR (90 MHz) 0.03 (s, CH_3Si), 0.86 (s, $(CH_3)_3C$), 0.96–1.55 (env, ring CH_2), 1.66–2.50 (m), 4.16 (AB q, $J = 11.7$ Hz, $\Delta\nu = 28.3$ Hz, trans CH_2O), 4.03 (s, cis CH_2O) ppm. GC/MS, *m/e* (M^+) 437, calcd (M^+) 436.8.

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Synthesis and Structure of Some Peri-Substituted 2,4,6,8-Tetraazabicyclo[3.3.0]octanes

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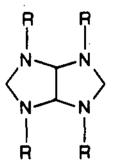
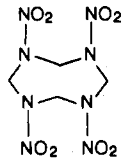
The synthesis and crystal structures of several substituted *cis*-2,4,6,8-tetraazabicyclo[3.3.0]octanes are reported. The stability of this ring system varies widely with the nature of the substituents present. Electrophilic substitution reactions on nitrogen are especially conducive to ring opening.

2,4,6,8-Tetraazabicyclo[3.3.0]octane-3,7-diones (glycolurils, **3**) have been investigated extensively and are often easily synthesized by condensation of ureas with glyoxal.[1] The parent ring compounds, the tetraazabicyclo[3.3.0]octanes, are far less well-known. A few 2,4,6,8-tetra-*n*-alkyl-2,4,6,8-tetraazabicyclo[3.3.0]octanes with *N*-methyl (**1a**), ethyl, and *n*-butyl substituents have been prepared by reduction of the corresponding glycolurils.[2a,b] *N*-Nitroso and *N*-nitro derivatives of this ring system, such as **1d**, are of interest as polycyclic analogues of the high-energy compound HMX (**2**). However, such compounds are unknown even though the corresponding 3,7-dione **3c** is readily available by nitration of glycoluril.[3]



1a. R=CH3
b: R=CH(CH3)2
c: R=acetyl
d: R=NO2



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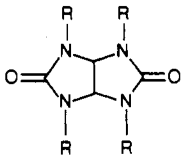

3a: R=CH3
b: R=CH(CH3)2
c: R=NO2

Initial synthesis efforts in our laboratory and elsewhere[4] indicated that the saturated tetraazabicyclooctane ring system **1** is not as easily formed by direct ring closure as the corresponding 3,7-diones. It appeared desirable to understand what structural factors affect its formation and stability. We now describe the synthesis, crystal structures, and selected properties of some potential precursors and structural analogues for **1d**.

Compounds **1a** and its higher *N*-alkyl homologues did not appear to be suitable precursors for **1d**, because no general method for replacement of *n*-alkyl by nitro exists. However, tertiary amines with *tert*-butyl or isopropyl groups undergo nitrolysis under mild conditions.[5] Therefore, the synthesis of **1b** and its *tert*-butyl analogue was attempted. *N*,*N*′-Diisopropylurea in the presence of acid readily condensed with glyoxal to a mixture of **3b** (≃50%) and *N*,*N*-diisopropylhydantoin (≃25%). The analogous reaction with *N*,*N*′-*tert*-butylurea was not successful. The glycoluril **3b** was reduced to **1b** with $LiAlH_4$ in dioxane at 90 °C. Pure **1b** can be stored in a closed container for a limited time. It is highly sensitive to acids.

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