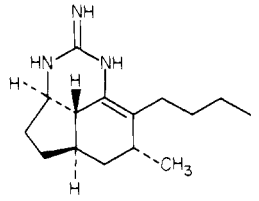
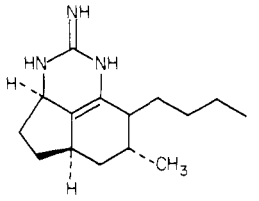
blesome, it proved, ultimately, to be of no major consequence to the successful completion of the syntheis.[16]

Benzylamino ketone **12a/12b** so obtained was smoothly deprotected, albeit again with considerable epimerization, via transfer hydrogenolysis (Pd black, 10% HCO_2H/CH_3OH, 23 °C, 1.5 h) to give the sensitive amino ketone **13a/13b** in 95% yield. Condensation of **13b** with the nitrate salt of 1-guanyl-3,5-dimethylpyrazole (GDMP)[17] (1 equiv, 120 °C, neat, 15 min) provided a ~1:1:2 mixture of three isomers (inseparable) tentatively assigned structures **14**, **15b**, and **2**, respectively, in 48% yield.[18] Under



14



15a,b

the same conditions **13a** afforded a mixture containing predominately **15a** and a small amount of **14**, but with only a trace of **2** present. Either mixture, however, could be equilibrated to **2** (89% after chromatography) by treatment with guanidine in refluxing C_6H_6 (12–24 h). Alternatively, treatment of **13a/13b** with 1.1 equiv of GDMP under equilibrating conditions (145–155 °C, neat, 6 h) afforded (−)-**2** directly in 58–65% yield. The ptilocaulin nitrate (mp 183–184 °C; $[\alpha]^{22}_D$ − 73.9° (*c* 0.31, 99.9% CH_3OH)) so obtained was identical in all respects (with the exception of optical rotation) with an authentic sample of the natural product.[19] The absolute configuration of (+)-ptilocaulin is thus established as that represented by **1**.

Acknowledgment. This research was generously supported by grants from the National Cancer Institute (Training Grant No. T32-CA-09112) and the National Science Foundation (Grant No. 8106987-CHE).

Registry No. 1, 78777-02-3; **2**, 88154-76-1; **2**·HNO_3, 88195-34-0; **3**, 13368-65-5; **4**, 88154-77-2; **4** (butylated), 88057-80-1; **5a**, 88154-78-3; **5b**, 88154-79-4; **6a**, 88154-80-7; **6a**-enol diethylphosphate, 88057-81-2; **6b**, 88155-70-8; **6b**-enol diethylphosphate, 88057-82-3; **7a**, 88057-64-1; **7b**, 88057-65-2; **8a**, 88057-66-3; **8b**, 88057-67-4; **9a**, 88057-68-5; **9b**, 88057-69-6; **10a**, 88057-70-9; **10b**, 88154-81-8; **11a**, 88057-71-0; **11a**·HCl, 88057-73-2; **11b**, 88057-72-1; **11b**·HCl, 88057-74-3; **12a**, 88057-75-4; **12a** (C-8b epimer), 88057-83-4; **12b**, 88057-76-5; **12b** (C-8b epimer), 88057-84-5; **13a**, 88057-77-6; **13a** (C-8b epimer), 88057-85-6; **13b**, 88057-78-7; **13b** (C-8b epimer), 88057-86-7; **14**, 88154-82-9; **15a**, 88057-79-8; **15b**, 88154-83-0; GDMP, 38184-47-3; benzylhydroxylamine, 622-30-0; **4** (butylated), 88057-80-1.

Supplementary Material Available: Spectroscopic data and physical constants for **5a,b, 6a,b, 7a,b, 8a,b, 9b, 10a,b, 11a,b, 12a,b, 13a,b,** and synthetic ptilocaulin (9 pages). Ordering information is given on any current masthead page.

(15) Greater amounts of epimerization occurred when the Jones oxidation of **11a/11b** was performed in aqueous acetone. The use of acetic acid as solvent greatly accelerated the rate of oxidation (this solvent effect has previously been noted: Mueller, R. H.; DiPardo, R. M. *J. Org. Chem.* **1977**, *42*, 3210), which allowed this step to be performed at 0 °C. Although the trans-fused epimers could be removed by chromatography, this separation proved unnecessary on a routine basis (see ref 16).

(16) The successful solution to this synthesis relies on thermodynamic control. Indeed, epimeric mixture of **12a/12b** brought through the sequence afford ptilocaulin by using the high-temperature GDMP step described in the text.

(17) Bannard, R. A. B.; Casselman, A. A.; Cockburn, W. F.; Brown, G. M. *Can. J. Chem.* **1958**, *36*, 1541.

(18) All compounds containing the guanidinium moiety were isolated and characterized as nitrate salts.

(19) Natural ptilocaulin nitrate has mp 183–185 °C (ref 2) and $[\alpha]^{23}_D$ +74.4° (99.5% CH_3OH) (Prof. K. L. Rinehart, personal communication). We thank Prof. Rinehart for providing the optical rotation data as well as a sample of natural ptilocaulin nitrate. We are also grateful to Prof. B. B. Snider for providing spectroscopic data and a sample of racemic **1**.

Synthesis of (*R*)-(+)-[10.10]- and -[22.10]Betweenanene and Related *trans*-Cyclododecenes

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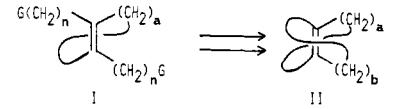
Contribution from the Department of Chemistry, University of South Carolina, Columbia, South Carolina 29208. *Received June 17, 1983*

Abstract: A general synthesis of 1,2-disubstituted *trans*-cycloalkenes is described starting from 2-methylenecyclododecanone. Addition of dimethylsulfonium methylide affords the vinyl oxirane **1** which undergoes highly selective S_N2' addition with organocopper reagents derived from alkylmagnesium bromides and copper(I) iodide in THF–Me_2S. The resulting *trans*-cyclododecenylcarbinols **2** are coupled via the diethyl phosphate derivatives **3** to the dialkylcyclododecenes **4**. Sharpless resolution of alcohols **2** leads via the same sequence to optically active cyclododecenes **4** of *R* configuration. A second coupling route entails oxidation of the alcohols **2** to aldehydes **12**, addition of Grignard reagents to give the allylic alcohols **13**, and Birch reduction of the derived acetates **14**. Conversion of the ω-alkenyl-substituted cyclododecenes **4b** and **14** to the dialdehydes **6** and **17** followed by McMurry Ti(0) cyclization and catalytic hydrogenation affords optically active [10.10]- and [22.10]betweenanene of *R* configuration.

The inherent chirality of *trans*-cycloalkenes was noted by Blomquist[1] in 1952 and experimentally confirmed some ten years later by Cope.[2] In a brilliant series of studies, Cope resolved

Scheme I



I II

trans-cyclooctene[2a] and correlated the (−)-enantiomer with (+)-tartaric acid thus establishing the absolute stereochemistry as (*R*)-(−).[2b,3] He also found that while *trans*-cyclononene could

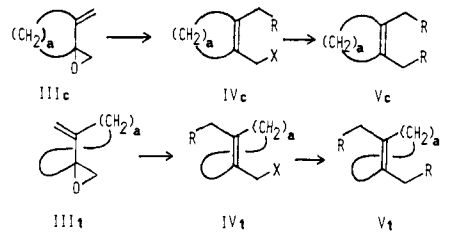
(1) Blomquist, A. T.; Liu, L. H.; Bohrer, J. C. *J. Am. Chem. Soc.* **1952**, *74*, 3643–7.

(2) (a) Cope, A. C.; Howell, C. F.; Knowles, A. *J. Am. Chem. Soc.* **1962**, *84*, 3190–1. Cope, A. C.; Ganellin, C. R.; Johnson, H. W. *Ibid.* **1962**, *84*, 3191–2. Cope, A. C.; Ganellin, C. R.; Johnson, H. W. Jr.; Van Auken, T. V.; Winkler, H. J. S. *Ibid.* **1963**, *85*, 3276–9. (b) Cope, A. C.; Mehta, A. S. *Ibid.* **1964**, *86*, 5626–30. (c) Cope, A. C.; Banholzer, K.; Keller, H.; Pawson, B. A.; Whang, J. J.; Winkler, H. J. S. *Ibid.* **1965**, *87*, 3644–9. (d) Cope, A. C.; Pawson, B. A. *Ibid.* **1965**, *87*, 3649–51. (e) Binsch, G.; Roberts, J. D. *Ibid.* **1965**, *87*, 5157–62.

(3) Cahn, R. S.; Ingold, C.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 385–415. See pp 400–3.

0002-7863/84/1506-0723$01.50/0

Scheme II



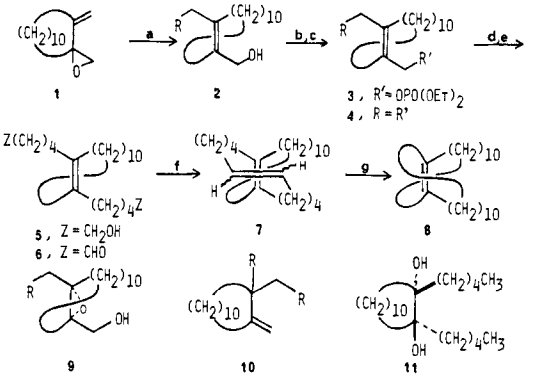
be resolved at low temperature, it rapidly racemizes at room temperature.[2c] *trans*-Cyclodecene could not be resolved even at low temperature and was presumed to be optically unstable. Using alkyl substituents to retard the racemization process,[2d,e] we were able to prepare optically active (−)-*trans*-1,2-dimethylcyclodecene (I; $a = 8$, $n = 1$, G = H) and (+)-*trans*-1,2-dimethylcycloundecene (I; $a = 9$, $n = 1$, G = H) from resolved bicyclo[5.2.1]undecenylcarbinyl and bicyclo[6.3.1]dodecenylcarbinyl (+)-camphorsulfonates[4] (see Scheme I). The former olefin was shown to possess the (*R*)-(−) configuration through correlation with (+)-(4a*S*)-4a-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalen-2-one.[5a] The present work was undertaken to develop a direct and general route to optically active *trans*-1,2-dialkylcycloalkenes (I) of known absolute configuration which, through appropriate choice of side chain substituents, could be converted to optically active betweenanenes (II).[5b]

Our plan (Scheme II) entailed the addition of an organocopper reagent to a vinyl spirooxirane (III) with the expectation that the favored transition state for the reaction would involve S_N2' substitution via the transoid conformer to give the *trans*-cycloalkenylcarbinol IVt (X = OH).[6] We have previously shown that such allylic alcohols can be cleanly resolved via Sharpless epoxidation[5,7] so the sequence can lead to optically active *trans*-cycloalkenes of predictable configuration. Homologation to the dialkylcycloalkene Vt would be possible through coupling of an allylic derivative IVt (X = leaving group) with an organometallic reagent.[6] Functionalization of the chain termini followed by cyclization would then give optically active betweenanenes (II) of known absolute configuration.

As an initial test of this plan we selected the twelve membered spiro vinyl oxirane **1** (see Scheme III), readily prepared from 2-methylenecyclododecanone[8] via condensation with dimethylsulfonium methylide.[9] Additions of organocopper reagents to vinyl oxiranes have been previously examined. Simple acyclic systems, such as butadiene and isoprene epoxide, give predominantly products of S_N2' displacement via the s-trans transition state (cf. IVt),[10] whereas cyclic vinyl oxiranes such as 1,3-cyclohexadiene monoepoxide give mixtures of S_N2 and S_N2' products via the obligatory s-cis transition state.[11,12] In the large ring exocyclic epoxide **1**, we expected conformational interconversion to be possible but we had no way of evaluating the probable transition state energies of the reactions leading to IVc vs. IVt.

To permit flexibility in alkyl group substitution we examined copper species derived from Grignard reagents[13] in our initial

Scheme III[a,b]



[a] (a) RMgBr, CuI, Me_2S, THF, −25 °C; (b) $ClPO(OEt)_2$, C_5H_5N; (c) RMgBr, CuI, Me_2S, THF, DME, −25 °C; (d) $(Me_2CHCH(Me))_2BH$, THF; H_2O_2, NaOH; (e) $CrO_3 \cdot HCl \cdot C_5H_5N$, CH_2Cl_2; (f) $TiCl_3$, Li, DME; (g) H_2/Pt-C, EtOAc. [b] a series, R = *n*-C_4H_9; b series, R = $(CH_2)_2CH{=}CH_2$; c series, R = $(CH_2)_9CH{=}CH_2$.

studies with vinyl oxirane **1**. Fujisawa observed that copper(I) iodide catalyzed additions of Grignard reagents to isoprene epoxide favored trans allylic alcohol products.[14] We found this to be the case with oxirane **1** as well, but yields were low. Eventually an efficient procedure was developed employing a 1:1 complex of Grignard reagent and copper(I) iodide in tetrahydrofuran-dimethyl sulfide. Allylic alcohols **2a–c** were thus prepared in over 90% yield. In each case less than 3% of the corresponding cis isomer (cf. IVc, X = OH) could be detected.

The trans allylic alcohols **2a–c** were readily identified through the characteristic AB pattern of their diasterotopic carbinyl protons in the ^1H NMR spectra. The corresponding protons of the cis isomers appeared as singlets with comparable chemical shifts. Ratios of cis/trans isomers, estimated through integration of these spectra, were confirmed by liquid chromatographic analysis.

Our next concern was the resolution of allylic alcohols **2b,c** using the Sharpless asymmetric epoxidation.[7] We previously found that a 10-membered analogue of alcohol **2** readily underwent enantioselective epoxidation with the (+)-diethyl tartrate derived reagent to give the epoxide derivative of the *R* olefin enantiomer and recovered *S* olefin.[5] We felt that similar selectivity would be possible with allylic alcohols **2b–c** provided the barrier to rotation of the ten-carbon bridging chain (jump rope rotation) past the CH_2OH grouping was high enough to prevent interconversion of the *R* and *S* enantiomers under the reaction conditions.[2e] In some earlier studies we concluded that *trans*-1,2-dimethylcyclododecene was capable of such rotation at room temperature.[4] However, since the steric requirements of CH_2OH should be greater than those of CH_3 the jump rope barrier should be higher for alcohols **2b–c**. This evidently proved to be the case since epoxidation of **2a** using the complex derived from *tert*-butyl hydroperoxide, titanium isopropoxide, and (+)-diethyl tartrate proceeded to 50% completion within 10 min to give the (*S*)-(+)-pentylcyclododecenylcarbinol (**2a**) in 41% isolated yield along with the (−)-epoxy alcohol **9a** in 50% isolated yield.[7] Epoxide **9a** proved prone to rearrangement and could not be readily purified. The pentenyl and dodecenyl allylic alcohols **2b** and **2c** gave rise to the (*S*)-(+)-carbinols **2b–c** and the unstable epoxides (−)-**9b–c** analogously.

The optical purity of alcohol (+)-**2b** was estimated by ^1H NMR analysis using the chiral shift reagent $Eu(facam)_3$.[15] Racemic **2b** gave rise to two AB quartets (carbinyl CH_2) of equal intensity upon addition of 0.37 molar equivalents of the reagent. With (+)-**2b**, under identical conditions, only a single AB quartet was discernible. On the basis of an estimated 5% threshold sensitivity

(4) Marshall, J. A.; Konicek, T. R.; Flynn, K. E. *J. Am. Chem. Soc.* **1980**, *102*, 3287–8.

(5) (a) Marshall, J. A.; Flynn, K. E. *J. Am. Chem. Soc.* **1982**, *104*, 7430–5. (b) For a review, see: Marshall, J. A. *Acc. Chem. Res.* **1980**, *13*, 213–18. (c) It should be noted that owing to a priority exchange of double bond substituents the (*S*)-alcohols **2** have the same chirality sense as the (*R*)-olefins **4–8**. We are indebted to David Huddle of CAS for calling this reversal to our attention.

(6) Magid, R. M. *Tetrahedron* **1980**, *36*, 1901–30.

(7) Sharpless, K. B.; Katsuki, T. *J. Am. Chem. Soc.* **1980**, *102*, 5974–6.

(8) Gras, J.-L. *J. Org. Chem.* **1981**, *46*, 3738–41. Kruizinga, W. H.; Kellogg, R. M. *J. Am. Chem. Soc.* **1981**, *103*, 5183–9.

(9) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353–64.

(10) Anderson, R. J. *J. Am. Chem. Soc.* **1970**, *92*, 4978–9. Johnson, C. R.; Herr, R. W. *Ibid.* **1970**, *92*, 4979–81.

(11) Rickborn, B.; Staroscik, J. *J. Am. Chem. Soc.* **1971**, *93*, 3046–7.

(12) Marino, J. P.; Abe, H. *J. Org. Chem.* **1981**, *46*, 5379–83.

(13) Unsaturated organolithium compounds such as 3-butenyllithium can react via their cyclic forms. Wakefield, B. J. "The Chemistry of Organolithium Compounds"; Pergamon Press: New York, 1974; pp 89–92.

(14) Fujisawa, T.; Sato, T.; Kawara, T.; Ohashi, K. *Tetrahedron Lett.* **1981**, *22*, 4823–6.

(15) For reviews of lanthanide NMR shift reagents see: (a) Siever, R. E.; Kime, K. A. *Aldrichimica Acta* **1977**, *10*, 54–62. (b) Cockerill, A. F.; Davies, G. L.; Harden, R. C.; Rackham, D. M. *Chem. Rev.* **1973**, *73*, 553–88.

for ^1H NMR peak detection, we judge (+)-**2b** to be at least 90% optically pure.

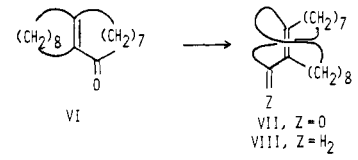
Evaluation of optical purity for the (*S*)-dodecenyl carbinol (+)-**2c** in the same manner was not successful. The addition of Eu(facam)$_3$ to racemic **2c** caused peak shifting but no splitting was observed. However, the Mosher's ester derivative **3c** (R′ = (+)-Ph(CF$_3$)(OMe)CCO$_2$) permitted an analysis to be made.[16] The ester derived from racemic **2c** gave rise to two well-resolved peaks in the ^{19}F NMR spectrum. The same derivative of alcohol (+)-**2c** displayed these two peaks in the ratio 98:2 and the ester derived from a 95:5 synthetic mixture of (+)-**2c** and racemic **2c** showed a 92:8 ratio. The optical purity of (+)-**2c** therefore exceeds 90%.

The next step in our synthetic route required the coupling of a derivative of allylic alcohols **2b** and **2c** with an appropriate ω-alkenyl grouping to give the betweenanene precursors, trienes **4b** and **4c**. While such coupling reactions are well documented,[6] no examples involving tetrasubstituted allylic systems such as **2** have been reported. Using the pentenyl system **2b** for initial studies, we examined a considerable number of allylic derivatives, including the acetate, xanthate,[17] chloride, phosphite, and phosphate, as well as the alcohol itself,[18] in combination with various organocopper species derived from 3-butenylmagnesium bromide. The major problems encountered were (1) rearrangement of the allylic derivative (chloride and xanthate), (2) elimination of the allylic derivative (chloride, xanthate and phosphate) and (3) unfavorable ratios of S_N2' (e.g., **10b**) to S_N2 displacement.[18b] Our best results were obtained with a 1:1 ratio of Grignard reagent and copper(I) iodide in 1,2-dimethoxyethane (DME)–dimethyl sulfide which led to a 4:1 mixture of **4b** and **10b** in 90% yield. However, when the 10-undecenyl Grignard reagent–copper(I) iodide complex was added to the dodecenyl-substituted allylic phosphate **3c**, the undesired S_N2' product **10c** was found to predominate 4:1. Interestingly, the 3-butenyl copper reagent mainly gave the S_N2 product **4c** (R = 3-butenyl) with phosphate **3c**. Thus the alkyl group in the copper reagent seems to exert remarkable control over the coupling regiochemistry. We examined a number of alternative coupling conditions with various combinations of leaving group and organocopper reagent but to no avail. The didodecenyl-substituted product **4c**, required for the synthesis of [22.10]betweenanene, was formed in only minor amounts at best. We were thus forced to consider alternative coupling strategies for the synthesis of this intermediate.

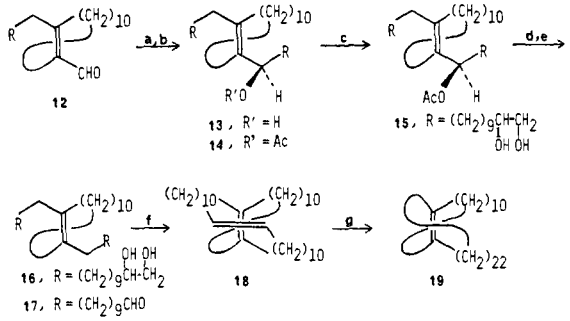
The plan we chose to explore entailed addition of the 10-undecenyl Grignard reagent to aldehyde **12c**, secured through oxidation of alcohol **2c**. Subsequent hydrogenolysis would lead to the desired intermediate **4c**. This plan calls into question the ability of a formyl group to block jump rope rotation in aldehydes such as **12** and it also requires that racemization does not take place in the subsequent hydrogenolysis step.

Feasibility studies on this approach were conducted with the pentyl-substituted (**a**) series. Oxidation of alcohol (+)-**2a** with manganese dioxide in benzene afforded the (+)-aldehyde **12a** quantitatively. This intermediate showed no loss of optical activity on storage. Hence the formyl group must be large enough to prevent rotation of the decamethylene bridge. Addition of *n*-butylmagnesium bromide to aldehyde (+)-**12a** afforded the allylic alcohol (+)-**13a**. This alcohol gave rise to only one set of signals in the ^{13}C NMR spectrum suggestive of a single diastereoisomer. Assuming attack by the Grignard reagent occurs anti to the bridging methylene chain on the transoid conformer of aldehyde (+)-**12a**, we assign the *R* configuration to the newly formed carbinol chiral center.

Scheme IV



Scheme V[a,b]



[a] (a) RMgBr, THF; (b) Ac_2O, C_5H_5N, 4-$Me_2NC_5H_4N$; (c) OsO_4, Me_3N-O, *t*-BuOH, acetone; $NaHSO_3$, H_2O; (d) Li, $EtNH_2$, THF; (e) $NaIO_4$, H_2O, dioxane; (f) $TiCl_3$, Li, DME; (g) H_2/Pt-C, EtOAc. [b] a series, R = *n*-C_4H_9; b series, R = $(CH_2)_2CH{=}CH_2$; c series, R = $(CH_2)_9CH{=}CH_2$).

The acetate derivative (+)-**14a** of alcohol (+)-**13a** was reduced with lithium in ethylamine to (*R*)-(+)-*trans*-1,2-dipentylcyclododecene (**4a**), $[\alpha]_D$ +43.6°. A comparison sample, $[\alpha]_D$ +46.5°, was prepared via hydrogenation of the (+)-dipentenyl compound **4b** using Wilkinson's catalyst.[19] Thus the two coupling routes proceed with comparable stereoselectivity.

The next stage of this project entailed conversion of the (*R*)-(+)-trienes **4b** and **4c** to (*R*)-[10.10]- and [22.10]betweenanenes (**8** and **19**). We were especially interested in the optical rotation of these olefins. Only two chiroptical studies have been carried out on such compounds. In the first, the trans enone VII (see Scheme IV), prepared via photoisomerization of the cis isomer VI in the presence of (+)-diethyl tartrate, was converted to (*R*)-(−)-[8.8]betweenanene (VIII), $[\alpha]_D$ −2.3° [20]. The CD spectrum of VIII was used to assign absolute stereochemistry. The optical purity was estimated to be 0.5–1% by comparison of the observed rotation with that of (*R*)-(−)-*trans*-cyclooctene ($[\alpha]_D$ −458°, $[\phi]$ −504°). The second such study was our kinetic resolution of [26.10]- and [22.10]betweenanene via enantioselective epoxidation.[21] Molecular rotations of 400–425° were estimated for these olefins. However, our measurement of optical purity was based on a ^{13}C NMR chiral shift reagent experiment which has been rendered suspect by work with diol **11** to be described shortly.

The synthesis of (*R*)-[10.10]betweenanene (**8**) from triene (+)-**4b** was completed along lines previously reported.[21,22] Thus, hydroboration–oxidation led to diol (+)-**5** which was oxidized by pyridinium chlorochromate to dialdehyde (+)-**6**. Slow addition of this dialdehyde to a suspension of reduced titanium(III) chloride in refluxing DME afforded diene **7** as a mixture of cis and trans disubstituted olefin isomers.[23] Hydrogenation over platinum on carbon gave (R)-(+)-[10.10]betweenanene (**8**), $[\alpha]_D$ +46.9° ($[\phi]$ +143°).

The synthesis of [22.10]betweenanene, shown in Scheme V, commenced with aldehyde (+)-**12c** obtained via oxidation of alcohol (+)-**2c** with manganese dioxide. Addition of 10-undecenylmagnesium bromide afforded the allylic alcohol (+)-**13c**.

(16) Mosher, H. S.; Dale, J. A.; Dull, D. L. *J. Org. Chem.* **1969**, *34*, 2543–9.

(17) There is no precedent for coupling of xanthates but examples are known for carbamates: Gallina, C.; Ciattini, P. G. *J. Am. Chem. Soc.* **1979**, *101*, 1035–6.

(18) (a) Tanigawa, Y.; Kanamaru, H.; Sonada, A.; Murahashi, S. I.; *J. Am. Chem. Soc.* **1977**, *99*, 2361–6. (b) For a more detailed discussion of these experiments see Flynn, K. E. Ph.D. Dissertation, Northwestern University, Evanston, IL, 1983.

(19) Wilkinson's catalyst is (tris(triphenylphosphine))rhodium(I) chloride. It is commercially available from Aldrich Chemical, Milwaukee, WI.

(20) Nakazaki, M.; Yamamoto, K.; Maeda, M. *J. Chem. Soc., Chem. Commun.* **1980**, 294–5.

(21) Marshall, J. A.; Black, T. H. *J. Am. Chem. Soc.* **1980**, *102*, 7581–3.

(22) Marshall, J. A.; Chung, K.-H. *J. Org. Chem.* **1979**, *44*, 1566–7.

(23) McMurry, J. E.; Fleming, M. P.; Kees, K. L.; Krepski, L. P. *J. Org. Chem.* **1978**, *43*, 3255–66. McMurry, J. E. *Org. Synth.* **1981**, *60*, 113–7.

The ^{13}C NMR spectrum of **13c**, like that of alcohol (+)-**13a**, showed a unique set of peaks consistent with a single diastereoisomer. Reduction of the acetate derivative (+)-**14c** with lithium in refluxing ethylamine afforded some of the desired triene **4c**, but the major product was the tetrahydro compound **4** (R = R′ = undecyl).[24] This unwanted double bond reduction did not occur at −78 °C, but then an appreciable quantity of alcohol **13c** was produced. Alcohol **13c** was also a major product in lithium–ammonia reductions of acetate (+)-**14c**.

This problem was easily circumvented through selective hydroxylation of the terminal olefins and then hydrogenolysis of the tetrol acetate **15** with lithium in ethylamine. Oxidative cleavage with sodium metaperiodate yielded the (+)-dialdehyde **17**. In our initial examination of this sequence we obtained dialdehyde **17** as a mixture of cis and trans isomers in low yield. This unexpected result was eventually traced to the sample of acetate (+)-**14c** which had apparently isomerized on storage. Some elimination also appears to have taken place. The cis–trans isomerization of acetate (+)-**14c** could occur via two successive allylic rearrangements. The allylic acetate (+)-**14b** exhibited similar behavior. We wished to examine the stereochemistry of this process with acetate **14a** but this substance could not be induced to rearrange even in the presence of acid.

Using freshly prepared acetate (+)-**14c** we were able to effect conversion to dialdehyde (+)-**17** in 52% overall yield. Cyclization with reduced titanium(III) chloride in refluxing DME afforded diene **18** (mainly trans)[23] which was selectively hydrogenated to (*R*)-(+)-[22.10]betweenanene (**19**), $[\alpha]_D$ +27.2° ($[\phi]$ +128°).

While the sequences described in Schemes III and V afforded the optically active (*R*)-betweenanenes (+)-**8** and (+)-**19**, we felt that additional proof of enantiomeric purity was needed before conclusions could be made regarding the optical properties of these olefins. We were specifically concerned that the allylic coupling **3b** → **4b** and the Birch reduction **15** → **16** might have proceeded with partial racemization. Both reactions could involve allylic radical or radical anion intermediates and the stereochemical integrity of such species was unknown to us. The close agreement in optical rotations between the (*R*)-(+)-dipentylcyclododecene **4a** obtained via the two sequences was reassuring but not totally persuasive in view of the possible similarity of reaction pathways. We therefore sought direct evidence for the optical purity of these coupling products.

The dipentyl system (+)-**4a** seemed best suited for these studies since we had prepared this olefin by both coupling sequences. As noted above, we recently carried out a kinetic resolution of [26.10]- and [22.10]betweenanene (II; $a = 26$, $b = 10$ and $a = 22$, $b = 10$) via partial epoxidation of the racemic olefins with (+)-peroxycamphoric acid.[21] The recovered olefins were treated with excess borane–THF and oxidized to alcohols with alkaline hydrogen peroxide. These alcohols were analyzed via ^{13}C NMR using the chiral shift reagent Eu(facam)$_3$ which caused apparent shifting and splitting of the carbinyl carbons.

Unfortunately, this methodology failed with olefin (+)-**4a**. Hydroboration–oxidation led in this case to a mixture of at least three alcohols shown to be primary and secondary by ^{13}C NMR analysis using the INEPT program; no tertiary alcohol was detected.[18b] Evidently, extreme steric crowding causes isomerization of the initial hydroboration product to take place under unusually mild conditions.[25]

Still wishing to employ chiral shift reagents and ^{13}C NMR to assess the optical purity of olefin (+)-**4a**, we turned to hydroxylation as a means for preparing a suitable derivative for analysis. Since catalytic hydroxylations are known to fail with highly substituted olefins,[26] we employed a stoichiometric procedure, but this approach was also unsuccessful. The olefin was unreactive. Interestingly, trimethylamine *N*-oxide was found to promote the stoichiometric hydroxylation as evidenced (TLC analysis) by the disappearance of the olefin.[27] Even then we did not isolate the expected diol **11** but obtained instead a deep purple oil along with a small amount of dione resulting from oxidative cleavage of the double bond. The colored oil was thought to be the cyclic osmate derivative of diol **11**.[28] Apparently steric factors strongly retard normal hydrolytic cleavage of this osmate.[29] Treatment of the presumed osmate with lithium aluminum hydride[30] in refluxing THF forced the issue and gave the highly crystalline diol (−)-**11** in 50% yield.

Chiral shift reagents are now routinely used for the determination of optical purity by ^1H NMR analysis[15] but examples employing ^{13}C NMR are rare.[31] A complicating factor in the ^{13}C experiment is the bidirectional nature of the induced shifts. Thus while ^1H NMR resonances tend to shift in one direction with a given shift reagent, ^{13}C resonances shift both upfield and downfield. Furthermore, the shift reagent itself introduces additional resonance peaks further complicating the spectrum.

Shift experiments with diol **11** were carried out under carefully controlled conditions. Successive additions of precisely measured quantities of Eu(facam)$_3$ to racemic diol **11** in deuteriochloroform caused immediate disappearance of the carbinyl resonance at 79.3 ppm and effected shifting of most of the signals and eventual splitting of a methylene signal at 24 ppm. The optically active diol (−)-**11** showed the same shifted peaks but no splitting could be discerned. A synthetic mixture of 80% (−)-**11** and 20% racemic **11**, treated identically, gave rise to a measurable (10%) shoulder on the low field side of the 24 ppm peak. The enantiomeric purity of diol (−)-**11** and the olefin precursor (+)-**4a** could therefore be estimated as greater than 80%. It thus appears that both the coupling reaction **3b** → **4b** and the Birch reduction **14a** → **4a** proceed without appreciable racemization. We assume that this is also the case for acetate **15**.

Rotational data for the *trans*-cyclododecenes prepared in this study are summarized in Table I. All resolutions were effected via Sharpless epoxidation of alcohols **2a–c** using natural (+)-diethyl tartrate as the chiral ligand and configurations are assigned accordingly.[5c] The molecular rotations of all save three fall in the range of +100° to +180°. The conjugating formyl groups of (+)-**12a** and (+)-**12b** strongly enhance the rotations, presumably the consequence of increased polarization.[32] Interestingly, the nonconjugated dialdehyde (+)-**6** shows an enhanced rotation as well, suggestive of through space polarization. The effect is absent in the related diol (+)-**5** and the longer chain dialdehyde (+)-**17**. It should be noted that the molecular rotations of these *trans*-cyclododecenes fall well short of *trans*-cyclooctene ($[\phi]$ 500°).[2] We have observed comparable (150–200°) molecular rotations with 1,2-disubstituted cycloundecenes as well.[4] Thus *trans*-cyclooctene possesses an anomolously high molecular rotation compared with unstrained *trans*-cycloalkenes. Our previously reported rotations for [26.10]- and [22.10]betweenanene[21] now appear to be erroneous, both in magnitude and sign. The results of the present study clearly show the (+)-enantiomer of [22.10]betweenanene to possess the *R* configuration and it seems likely that the [26.10] analogue will follow suit. We are unable to offer a satisfactory explanation for the discrepancy. In reexamining the samples prepared in our earlier study[21] we have found significant impurities, possibly the result of prolonged storage.

(24) Benkeser, R. A.; Robinson, R. E.; Sauve, D. M.; Thomas, O. H. *J. Am. Chem. Soc.* **1955**, *77*, 3230.
(25) Cf. Brown, H. C.; Racherla, U. S. *J. Org. Chem.* **1983**, *48*, 1389–1391. Brown, H. C.; Racherla, U. S.; Taniguchi, H. *Ibid.* **1981**, *46*, 4313–4314.
(26) Akashi, K.; Palermo, R. E.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 2063–66.
(27) Amine oxides are known to activate Fe(CO)$_5$ towards complexation with dienes: Eekhof, J. H.; Hogeveen, H.; Kellogg, R. M. *J. Chem. Soc. Chem. Commun.* **1976**, 657.
(28) Criegee, R. *Liebigs Ann. Chem.* **1936**, *522*, 75–96.
(29) Criegee, R.; Marchand, B.; Wannowius, H. *Liebigs Ann. Chem.* **1942**, *550*, 99–133.
(30) Castells, J.; Meakins, G. D.; Swindells, R. *J. Chem. Soc.* **1962**, 2917–24.
(31) An early publication in this area noted the splitting of ^{13}C resonances by Eu(facam)$_3$ in racemic materials but did not actually determine optical purity by this method: Fraser, R. R.; Stothers, J. B.; Tan, C. T. *J. Magn. Reson.* **1973**, *10*, 95–7. For studies on olefin–silver complexes with chiral shift reagents see: Offermann, W.; Mannschreck, A. *Tetrahedron Lett.* **1981**, *22*, 3227–30.
(32) Cf. Brewster, J. H. *Tetrahedron* **1961**, *13*, 106–22.

Unfortunately the amount of material on hand proved insufficient for detailed analysis.

It is worth noting that the allylic alcohols **2b–c** and the olefins **4b**, **8**, and **19** exhibit negative CD Cotton effects in accord with the predictions of Scott and Wrixon.[33] A series of 1,2-dimethyl-*trans*-cycloundecenes and -cyclodecenes of *R* configuration likewise showed negative Cotton effects.[4,34] Thus the Scott–Wrixon olefin octant rule appears valid for olefins whose sole asymmetry arises from planar chirality.

Experimental Section[35]

4-Methylene-1-oxaspiro[2.11]tetradecane (1). The procedure of Corey[9] was modified. To a mechanically stirred, cooled (−20 °C) slurry of 92.7 g (0.454 mol) of trimethylsulfonium iodide (recrystallized from 95% ethanol) and 100 mL (0.6 mol) of hexamethylphosphoramide in 400 mL of tetrahydrofuran (THF) was added, dropwise, 284 mL (0.454 mol) of 1.60 M methyllithium in THF (low halide content). After the addition was complete the mixture was stirred for 15 min. Then 44.0 g (0.227 mol) of 2-methylenecyclododecanone was added at −20 °C. After 1 h the reaction mixture was poured into water and extracted with ether. The combined ethereal extracts were washed with water, saturated sodium thiosulfate, and brine and dried over anhydrous potassium carbonate. Removal of solvents gave 52 g of a crude orange oil which was chromatographed on a Waters Prep 500 HPLC (1% ethyl acetate–hexane) to give 19 g (40%) of vinyl oxirane **1** as a clear colorless oil: IR (film) ν 3075, 3025, 2925, 2850, 1640, 1480, 1460, 920 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.1–1.7 (m), 2.05 (m), 2.6 (s), 5.0 (s, C=CH), 5.15 (s, C=CH). Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.90; H, 11.61.

(±)-(*E*)-1-(Hydroxymethyl)-2-(4-pentenyl)cyclododecene (2b). The procedure of Fujisawa was modified.[14] To a mechanically stirred, cooled (−78 °C) solution of 27.5 g (0.144 mol) of copper(I) iodide (THF washed) in 64.5 mL (0.878 mol) of dimethyl sulfide and 250 mL of THF under argon was added dropwise 91 mL (0.144 mol) of 1.58 M 3-butenylmagnesium bromide in THF. The resultant red-orange precipitate was stirred at −78 °C for 15 min. A solution of 15 g (71.1 mmol) of vinyl oxirane **1** in 50 mL of THF was added dropwise with stirring to give a blood-red precipitate. The reaction flask and bath were placed in a freezer (−25 °C) overnight. The final blue-black solution was poured into a mixture of saturated ammonium chloride and ammonium hydroxide and extracted with ether. The combined organic layers were washed with 3% ammonium hydroxide (until the washes were colorless), water, and brine and dried over anhydrous magnesium sulfate. Removal of solvents at reduced pressure gave 19.62 g of the crude allylic alcohol **2a** as an oil. Analytical HPLC showed this crude product to contain 3% of the cis allylic alcohol. Purification by chromatography (silica gel, 10% ethyl acetate–hexane) afforded 18.8 g (99%) of the allylic alcohol **2a** as a clear colorless oil: IR (film) ν 3300, 3060, 2925, 2850, 1645, 1480, 1005, 920 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.0–1.6 (m), 1.6–2.6 (m), 4.10 (s, CH_2OH, cis isomer), 4.18 (ABq, $\Delta\nu$ = 49.6 Hz, J_{AB} = 12 Hz, CH_2OH, trans isomer), 4.85–5.15 (m, C=CH_2), 5.55–6.0 (m, CH=CH_2); ^{13}C NMR ($CDCl_3$) δ 138.9, 138.6, 133.9, 114.4, 61.5, 33.7, 31.8, 29.9, 29.6, 28.4, 27.9, 26.33, 26.31, 26.0, 25.6, 24.6, 24.5. Anal. Calcd for $C_{18}H_{32}O$: C, 81.75; H, 12.20. Found: C, 81.77; H, 12.11.

(±)-(*Z*)-1-(Hydroxymethyl)-2-pentylcyclododecene (2a). The procedure outlined for the preparation of alcohol **2b** was followed by using 18.2 g (96.2 mmol) of copper(I) iodide, 80.2 mL (96.2 mmol) of 1.2 M butylmagnesium bromide in THF, and 42.2 mL (0.577 mol) of dimethyl sulfide in 175 mL of THF with 10 g of (48.1 mmol) vinyl oxirane **1**. Workup afforded 12.8 g (100%) of the pentyl allylic alcohol **2a** as a crystalline solid: mp 64–65 °C; IR (film) ν 3350, 2950, 2850, 1480, 1390, 1080, 1020 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.9 (t, CH_3CH_2), 1.0–1.6 (m), 2.05–2.6 (m), 4.2 (ABq, $\Delta\nu$ = 49.6 Hz, J_{AB} = 12 Hz, CH_2OH); ^{13}C NMR ($CDCl_3$) δ 139.5, 133.5, 61.6, 32.4, 32.0, 29.9, 28.9, 27.8, 26.3, 26.0, 25.6, 24.5, 24.4, 22.6, 14.0. Anal. Calcd for $C_{18}H_{34}O$: C, 81.13; H, 12.86. Found: C, 81.00; H, 12.93.

(±)-(*Z*)-1-(Hydroxymethyl)-2-(11-dodecenyl)cyclododecene (2c). The procedure outlined for the preparation of alcohol **2b** was followed by using 9.16 g (48.08 mmol) of copper(I) oxide (THF washed), 68.6 mL (48.08 mmol) of 0.70 M 10-undecenylmagnesium bromide in THF and 21.2 mL (0.288 mol) of dimethyl sulfide in 80 mL of THF with 5 g (24.04 mmol) of vinyl oxirane **1**. Workup as before gave 13.7 g of a crude mixture of allylic alcohol and undecane. Purification by chromatography (silica gel, 10% ethyl acetate–hexane) afforded 7.8 g (90%) of dodecenyl allylic alcohol **2c** as a clear oil: IR (film) ν 3300, 3050, 2900, 2825, 1640, 990, 905 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.0–1.7 (m), 1.8–2.1 (m), 2.1–2.65 (m), 4.25 (ABq, $\Delta\nu$ = 46.5 Hz, J_{AB} = 12 Hz), 5.95 (m, C=CH_2), 5.75 (m, CH=CH_2); ^{13}C NMR ($CDCl_3$) δ 139.3, 139.0, 133.5, 114.0, 61.4, 33.7, 32.5, 30.0, 29.9, 29.6, 29.4, 29.3, 29.1, 28.9, 27.7, 26.31, 26.26, 26.0, 25.6, 24.5, 24.4. Anal. Calcd for $C_{25}H_{46}O$: C, 82.80; H, 12.79. Found: C, 82.56; H, 12.64.

(*S*)-(+)-(*E*)-1-(Hydroxymethyl)-2-(4-pentenyl)cyclododecene (2b). The procedure of Sharpless was modified.[7] To a cooled (−23 °C) flask

Table I. Rotations of *trans*-Cyclododecenes

compd	rotations [α], deg	rotations [ϕ], deg	CD curves λ_{max}, nm	CD curves sign
	Allylic Alcohols			
2a	+66.4	+177		
2b	+60.6	+160	221.5	−
2c	+47.8	+173	221	−
13a	+32.0	+103		
13c	+23.0	+118		
	Allylic Acetates			
14a	+30.2	+110		
14c	+27.2	+151		
	Conjugated Aldehydes			
12a	+103.6	+273		
12c	+97.9	+352		
	Diol, Dialdehydes			
5	+30.3	+102		
6	+103.6	+258		
17	+97.9	+104		
	Olefins			
4a	+46.5	+142		
4b	+50.6	+153	216.5	−
8	+46.9	+143	221	−
19	+27.2	+128	~220	−

(33) Scott, A. I.; Wrixon, A. D. *Tetrahedron* **1970**, *26*, 3695–3715.

(34) Flynn, K. E. Ph.D. Dissertation, Northwestern University, Evanston, IL, 1983, pp 32–40.

(35) (a) The apparatus and methods described by G. W. Kramer, M. M. Midland, and A. B. Levy [Brown, H. C. "Organic Syntheses via Boranes"; Wiley: New York, 1975; pp 191–202] were used to maintain an argon or nitrogen atmosphere in the reaction flask. (b) Isolation of reaction products was accomplished by pouring the reaction mixture into water and thoroughly extracting with the specified solvent. The combined organic extracts were washed with water until neutral. Pyridine was removed by washing with saturated aqueous copper(II) sulfate. The resulting organic solution was washed with saturated aqueous sodium chloride (brine), then dried over anhydrous magnesium sulfate (unless otherwise specified), and filtered, and the solvents were removed by distillation at reduced pressure on a Büchi Rotovapor. (c) Anhydrous solvents were obtained by distillation from sodium benzophenone ketyl (diethyl ether, tetrahydrofuran, 1,2-dimethoxyethane, and dioxane), calcium hydride (dichloromethane and hexamethylphosphoramide), or sodium (benzene and toluene). (d) Infrared spectra were determined with a Perkin-Elmer 727B spectrophotometer. Infrared absorption maxima are reported in wavenumbers (cm^{-1}) and are standardized by reference to the 1601 cm^{-1} peak of polystyrene. (e) Proton magnetic resonance spectra were recorded on EM-360A, IBM NR-80, and Varian EM-390 spectrometers. Carbon-13 spectra were recorded at 20 MHz on an IBM NR-80 Fourier transform spectrometer. All samples were prepared as dilute solutions in deuteriochloroform ($CDCl_3$). Chemical shifts (δ) are reported downfield from tetramethylsilane (Me_4Si), in parts per million (ppm) of the applied field. ^{19}F NMR spectra were recorded on a Bruker WP-200 spectrometer at 188.28 MHz. Resonances are reported downfield from trifluoroacetic acid. Peak multiplicities are abbreviated: singlet s, doublet d, triplet t, quartet q, and multiplet m. Coupling constants (J) are reported in Hertz (Hz). (f) Melting points were determined on a Fisher-Johns hot stage or a Thomas-Hoover capillary apparatus and are uncorrected. Boiling points are uncorrected. (g) Gas chromatography–mass spectral analysis (GC/MS) was performed on a Finnigan 4021 instrument. High-resolution mass spectra (HRMS) were determined at the Midwest Center for Mass Spectrometry, University of Nebraska, Lincoln, NE. (h) Combustion microanalyses were performed by Micro-Tech Laboratories, Inc., Skokie, IL. (i) Analytical thin-layer chromatography (TLC) was routinely used to monitor reactions. Plates precoated with E. Merck silica gel 60 F254 of 0.25-mm thickness, supplied by Brinkmann Instruments, were used. (j) Analytical gas–liquid chromatography (GLC) was performed with a Hewlett-Packard 5710A instrument equipped with a flame ionization detector and Model 3380A integrator, employing nitrogen as the carrier gas. (k) Analytical high-performance liquid chromatography (HPLC) was performed on an IBM LC/9533 chromatograph equipped with an IBM LC/9540 data integrator. Preparative liquid chromatography (LC) was performed on a Waters Prep LC/System 500 instrument equipped with silica gel columns. Column chromatography was performed using E. Merck silica gel 60 (230–400 ASTM mesh) according to the procedure of W. C. Still, M. Kahn, and A. Mitra (*J. Org. Chem.* **1978**, *43*, 2923–5).

containing 200 mL of dichloromethane was added dropwise, with stirring, 15.77 mL (53.0 mmol) of titanium tetraisopropoxide and 11 mL (64.0 mmol) of (+)-diethyl tartrate. After 5 min, 14 g (53.0 mmol) of (±)-alcohol **2b** in 50 mL of dichloromethane, and 8.86 mL (29.0 mmol) of 3.29 M *tert*-butyl hydroperoxide in 1,2-dichloroethane was added. After 10 min a small aliquot of the reaction was quenched in 10% tartaric acid and dried over sodium carbonate. Analysis by HPLC showed that the epoxidation had gone to 50% completion. The reaction was quenched at −26 °C with 125 mL of 10% tartaric acid (total reaction time was 30 min). After 15 min the mixture was allowed to warm to room temperature and stirring was continued until the aqueous layer was clear (1 h). The layers were separated and the aqueous layer was extracted once with dichloromethane. The combined organic layers were dried over potassium carbonate. Removal of solvent at reduced pressure gave 27 g of an orange oil which was chromatographed (Waters Prep 500 HPLC, 5% ethyl acetate–hexane) to give 5.45 g (39%) of (*R*)-(+)-**2b** and 4.6 g (31%) of (2*S*,3*S*)-(−)-**9b**.

(+)-**2b**: IR (film) ν 3300, 3060, 2925, 2850, 1645, 1480, 1005, 920 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.0–1.6 (m), 1.6–2.6 (m), 4.18 (ABq, $\Delta\nu$ = 46.5 Hz, J_{AB} = 12 Hz, CH_2OH), 4.95 (m, CH=CH_2), 5.75 (m, CH=CH_2); ^{13}C NMR ($CDCl_3$) δ 138.9, 138.6, 133.9, 114.4, 61.5, 33.7, 31.8, 29.9, 29.6, 28.4, 27.9, 26.33, 26.31, 26.0, 25.6, 24.6, 24.5; $[\alpha]^{29}_D$ +60.6° (*c* 3.33, $CHCl_3$). Anal. Calcd for $C_{18}H_{32}O$: C, 81.75; H, 12.20. Found: C, 81.46; H, 12.09.

(−)-**9b**: IR (film) ν 3400, 3050, 2900, 2850, 1640, 1465, 1040, 1000, 910 cm^{-1}; ^{1}H NMR δ ($CDCl_3$) 1.0–1.7 (m), 1.7–2.5 (m), 3.7 (m, CH_2–O–), 4.95 (m, CH=CH_2), 5.75 (m, CH=CH_2); ^{13}C NMR ($CDCl_3$) δ 138.2, 114.5, 69.2, 68.9, 63.2, 33.7, 31.3, 28.8, 27.9, 27.8, 27.7, 24.6, 24.5, 24.3, 23.9, 23.4; $[\alpha]^{29}_D$ −48.7° (*c* 4.13, $CHCl_3$). Anal. Calcd for $C_{18}H_{32}O_2$: C, 77.09; H, 11.50. Found: C, 77.28; H, 11.48.

(*S*)-(+)-(*Z*)-1-(Hydroxymethyl)-2-pentylcyclododecene (2a). The procedure described for the resoltuion of (+)-**2b** was followed by using 1.12 mL (3.76 mmol) of titanium tetraisopropoxide, 0.930 g (4.51 mmol) of (+)-diethyl tartrate, 1 g (3.76 mmol) of (±)-alcohol **2a**, and 0.69 mL (2.26 mol) of 3.29 M *tert*-butyl hydroperoxide in 1,2-dichloroethane and 20 mL of dichloromethane. After 20 min the reaction was quenched with 15 mL of 10% tartaric acid solution. Purification by chromatography gave 0.41 g (41%) of alcohol (+)-**2a** as needles, mp 61–63 °C, and 0.526 g (49%) of epoxide **9a** as a clear, colorless thick oil.

(+)-**2a**: IR (film) ν 3350, 2950, 2850, 1480, 1390, 1080, 1020 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.9 (t, CH_3CH$_2$), 1.0–1.6 (m), 2.05–2.6 (m), 4.2 (ABq, $\Delta\nu$ = 49.6 Hz, J_{AB} = 12 Hz, CH_2–OH); ^{13}C NMR ($CDCl_3$) δ 139.5, 133.5, 61.6, 32.4, 32.0, 29.9, 28.9, 27.8, 26.3, 26.0, 25.6, 24.5, 24.4, 22.6, 14.0; $[\alpha]^{22}_D$ +66.4° (*c* 1.76, $CHCl_3$). Anal. Calcd for $C_{18}H_{32}O$: C, 81.13; H, 12.86. Found: C, 81.32; H, 12.83.

A sample of alcohol (+)-**2a**, prepared via hydrogenation of alcohol (+)-**2b** over Wilkenson's catalyst in 86% yield, showed $[\alpha]^{22}_D$ +66.7° (*c* 0.54, $CHCl_3$).

9a: IR (film) ν 3350, 2900, 2850, 1460, 1040, 900 cm^{-1}; ^{1}H NMR 80 MHz ($CDCl_3$) δ 0.95 (t, *J* = 5 Hz, CH_3CH$_2$), 1.0–1.7 (m), 1.8–2.7 (m), 2.6 (m), 3.6 (m); ^{13}C NMR ($CDCl_3$) δ 69.3, 68.3, 63.3, 32.1, 31.9, 28.8, 27.9, 27.8, 27.7, 24.5, 24.4, 24.3, 23.9, 23.4, 22.5, 13.8.

(*S*)-(+)-(*Z*)-1-(Hydroxymethyl)-2-(11-dodecenyl)cyclododecene (2c). The procedure described for the resolution of (±)-**2b** was followed by using 4.0 g (11.05 mmol) of (±)-allylic alcohol **2c**, 3.29 mL (11.05 mmol) of titanium tetraisopropoxide, 2.74 g (13.3 mmol) of (+)-diethyl tartrate, 2.01 mL (6.63 mmol) of 3.29 M *tert*-butyl hydroperoxide in 1,2-dichloroethane solution, and 50 mL of dichloromethane.

Purification by chromatography (silica gel, 10% ethyl acetate–hexane) afforded 1.66 g (42%) of allylic alcohol (+)-**2c** and 1.57 g (35%) of (2*S*,3*R*)-epoxy alcohol (−)-**9c**.

(+)-**2c**: IR (film) ν 3300, 3050, 2900, 2825, 1640, 1460, 1440, 990, 910 cm^{-1}; ^{1}H NMR 60 MHz ($CDCl_3$) δ 1.0–1.7 (m), 1.7–2.7 (m), 4.2 (ABq, $\Delta\nu$ = 33.9 Hz, J_{AB} = 12 Hz), 4.95 (m, CH=CH_2), 5.75 (m, CH=CH_2); ^{13}C NMR ($CDCl_3$) δ 139.4, 139.1, 133.5, 114.0, 61.55, 33.75, 32.4, 30.25, 29.9, 29.8, 29.6, 29.4, 29.3, 29.1, 28.9, 27.8, 26.3, 26.0, 25.6, 24.5, 24.4; $[\alpha]^{24}_D$ +46.9° (*c* 2.35, $CHCl_3$). Anal. Calcd for $C_{25}H_{46}O$: C, 82.80; H, 12.79. Found: C, 83.15; H, 12.61.

(−)-**9c**: IR (film) δ 3350, 2900, 2850, 1640, 1470, 1040, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.2–1.75 (m), 1.8–2.3 (m), 3.75, (m, CH_2–O), 4.95 (m, CH=CH_2), 5.75 (m, CH=CH_2); ^{13}C NMR ($CDCl_3$) δ 139.1, 114.2, 69.7, 69.0, 63.6, 33.9, 32.3, 30.2, 30.0, 29.8, 29.7, 29.6, 29.5, 29.3, 29.1, 28.5, 28.3, 28.1, 25.0, 24.95, 24.9, 24.7, 24.6, 24.3, 23.7; $[\alpha]^{24}_D$ −58.1° (*c* 4.82, $CHCl_3$). Anal. Calcd for $C_{25}H_{46}O_2$: C, 79.30; H, 12.25. Found: C, 79.33; H, 12.30.

Mosher's Ester of (±)-(*Z*)-1-(Hydroxymethyl)-2-(11-dodecenyl)-cyclododecene 2c. The procedure of Sharpless was followed.[7] To a stirred solution of 0.360 g (0.99 mmol) of (±)-alcohol **2c** and 0.134 g (1.1 mmol) of 4-(dimethylamino)pyridine in 2.0 mL of dichloromethane was added 0.254 g (1.0 mmol) of (+)-α-methoxy-α-(trifluoromethyl)-phenylacetyl chloride in 1.0 mL of dichloromethane. After a few minutes the mixture was poured into ether and water, the aqueous layer was extracted with ether, the combined organic layers were washed with 10% hydrochloric acid, saturated sodium bicarbonate, and brine and dried over magnesium sulfate. Removal of solvents gave 0.487 g (85%) of the diastereomeric ester mixture as an oil: ^{1}H NMR ($CDCl_3$) δ 1.0–1.65 (m), 1.7–2.1 (m), 2.1–2.6 (m), 3.45 (s, OCH_3), 4.9 (ABq, $\Delta\nu$ = 46.5 Hz, J_{AB} = 12 Hz, CH_2–OCO–), 4.9 (m, CH=CH_2), 5.75 (m, CH=CH_2), 7.45 (m); ^{13}C NMR ($CDCl_3$) δ 166.3, 166.2, 143.9, 143.7, 138.9, 132.6, 129.2, 128.1, 127.4, 127.3, 127.2, 114.0, 65.2, 55.2, 33.7, 32.7, 31.8, 30.6, 29.5, 29.2, 29.1, 29.0, 28.9, 28.2, 28.0, 26.1, 25.9, 25.25, 24.8, 24.7, 24.5, 24.2, 22.6, 13.9; ^{19}F NMR ($CDCl_3$) δ 3.95, 4.0; ratio 7.6:7.7.

Mosher's Ester of (*S*)-(+)-(*Z*)-1-(Hydroxymethyl)-2-(11-dodecenyl)cyclododecene (2c). To a stirred solution of 0.126 g (0.348 mmol) of alcohol (+)-**2c** ($[\alpha]_D$ +46.0°) and 0.045 g (0.370 mmol) of 4-(dimethylamino)pyridine in 2 mL of dichloromethane was added via syringe 0.088 g (0.35 mmol) of (+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride dropwise. After a few minutes the reaction was quenched by the slow, dropwise addition of water and the reaction mixture was poured into water and extracted with ether. The combined ethereal layers were washed with 10% hydrochloric acid, saturated sodium bicarbonate, and brine and dried over magnesium sulfate. Removal of solvents gave 0.177 g (79%) of the ester as an oil: ^{19}F NMR ($CDCl_3$) (138.5 mg) δ 3.93, 4.04; integrated ratio 2:98. A 15.4-mg sample of ester derived from racemic **2c** was added to this NMR sample to make a 5:95 synthetic mixture: ^{19}F NMR ($CDCl_3$) δ 3.93, 4.04; integrated ratio of 8:92.

(*R*)-(+)-(*E*)-1,2-Di-4-pentenylcyclododecene (4b). The procedure of Alewood was modified.[36] To a stirred, cooled (−40 °C) solution of 4.92 mL (34.08 mmol) of freshly distilled diethyl chlorophosphate in 50 mL of pyridine was added dropwise 3 g (11.36 mmol) of allylic alcohol (+)-**2b** in 10 mL of pyridine. The reaction mixture was allowed to warm to −15 °C. After 2 h TLC showed no allylic alcohol so the reaction was quenched with 15 mL of water and extracted with ether. The ethereal layers were washed several times with saturated copper sulfate solution, water, and brine and dried over potassium carbonate. Removal of solvents at reduced pressure gave 3.58 g (79%) of **3b** as a yellow oil which was used *immediately* without further purification: IR (film) ν 3050, 2900, 2825, 1640, 1460, 1440, 1390, 1370, 1270, 1170, 1100, 1070, 1040, 1000, 910, 820, 800 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.0–1.3 (m), 1.3–1.5 (m, $POCH_2CH_3$), 1.6–2.7 (m), 4.07 (m, $POCH_2CH_3$), 4.65 (ABq, $\Delta\nu$ = 33 Hz, J_{AB} = 9 Hz, CH_2–O), 4.9 (m, CH=CH_2), 6.7 (m, CH=CH_2).

To a mechanically stirred, cooled (−78 °C) solution of 3.41 g (17.9 mmol) of THF-washed copper(I) iodide and 7.9 mL (0.107 mol) of distilled dimethyl sulfide in 65 mL of 1,2-dimethoxyethane (DME) was added dropwise 20.2 mL (17.9 mmol) of 0.88 M 3-butenylmagnesium bromide in THF. A rust-red precipitate quickly formed. After 15 min, the crude allylic phosphate **3b** was added in 10 mL of DME. After 15 min at −78 °C, the reaction flask and cooling bath were stored at −25 °C overnight. The resultant fine black slurry was poured into a mixture of saturated ammonium chloride and ammonium hydroxide and extracted with ether. The combined ethereal layers were washed with 3% ammonium hydroxide, water, and brine and dried over magnesium sulfate. Removal of solvents at reduced pressure gave 4.2 g of a crude oil. Analysis by GC showed this to be a 80:20 mixture of **3b** and **10b**. Column chromatography in two batches (1.5 L of Merck 60 silica gel, hexane) gave 1.24 g (46%) of (+)-**4b** and 1.3 g of a mixture of (+)-**4b** and **10b**.

(+)-**4b**: IR (film) ν 3075, 2900, 2850, 1640, 1380, 1000, 920 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.0–1.7 (m), 1.7–2.2 (m), 2.2–2.7 (m), 4.95 (m, CH=CH_2), 5.75 (m, CH=CH_2); ^{13}C NMR ($CDCl_3$) δ 139.0, 134.0, 114.2, 33.8, 31.4, 29.6, 28.8, 26.2, 25.8, 24.8; $[\alpha]^{29}_D$ +50.6° (*c* 3.65, $CHCl_3$); GC–MS M^+ 302. Anal. Calcd for $C_{22}H_{38}$: C, 87.34; H, 12.66. Found: C, 87.37; H, 12.91.

(*R*)-(+)-(*E*)-1,2-Dipentylcyclododecene (4a). A. **From (*S*)-(+)-(*Z*)-Acetate 14a.** To 20 mL of refluxing, anhydrous ethylamine was added 0.142 g (20.5 mmol) of lithium wire (cut into 2–3 mm pieces) with stirring. After 40 min, a solution of 0.163 g (0.45 mmol) of acetate (+)-**14a** in 5 mL of THF was added. After 4 h, the reaction was quenched with solid ammonium chloride and the mixture was poured into 10% hydrochloric acid. The aqueous layer was extracted with hexane. The combined organic layers were washed with water and saturated sodium bicarbonate and dried over anhydrous magnesium sulfate. Removal of solvents gave a crude oil which was chromatographed (silica gel, hexane) to afford 0.095 g (69%) of (*R*)-(+)-**4a** as a clear colorless oil: IR (film) ν 2900, 2925, 1475, 1370 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.85 (t, CH_3CH$_2$, *J* = 5 Hz), 1.1–1.6 (m), 1.6–2.1 (m), 2.1–2.6 (m); ^{13}C NMR ($CDCl_3$) δ 134.0, 32.0, 31.9, 29.6, 29.15, 26.3, 25.85, 25.1 24.95, 22.75,

(36) Alewood, P. E.; Perich, J. W.; Johns, R. R. *Synth. Commun.* **1982**, *12*, 821–8.

14.1; $[\alpha]_D$ +43.6° (*c* 1.93, $CHCl_3$); GC–MS M^+ 306, coinjection with the sample from part B gave a single peak. Anal. Calcd for $C_{22}H_{42}$: C, 86.19; H, 13.81. Found: C, 86.44; H, 13.87.

B. From (*R*)-(+)-Triene 4b. A slurry of 10 mg (0.011 mmol) of (tris(triphenylphosphine))-rhodium chloride in 2 mL of acetone was preequilibrated under a hydrogen atmosphere.[19] To this mixture was added a solution of 0.228 g (0.754 mmol) of triene (+)-**4b** in 1 mL of benzene. The resulting orange homogeneous solution was stirred vigorously under a hydrogen atmosphere for 7.5 h. The mixture was concentrated under reduced pressure and filtered through alumina with hexane. Removal of solvents gave 0.216 g (94%) of (+)-**4b** as a clear, colorless oil: IR (film) ν 2900, 2825, 1475, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (t, CH_3CH_2, J = 5 Hz, 6 H), 1.1–1.6 (m), 1.6–2.1 (m, 4 H), 2.1–2.6 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 134.0, 32.0, 31.9, 29.5, 29.2, 26.3, 25.9, 25.0, 24.9, 22.8, 14.1; $[\alpha]^{27}_D$ +46.5° (*c* 2.16, $CHCl_3$).

(*R*)-(+)-1,2-Bis(4-hydroxypentyl)cyclododecene (5). The procedure of Brown was followed.[37] To a stirred, cooled (−10 °C) solution of 17.1 mL (17.1 mmol) of 1 M borane in THF was added by automatic syringe over 30 min 3.8 mL (35.9 mmol) of 2-methyl-2-butene in 10 mL of THF. The reaction mixture was warmed to 0 °C and stirred for 1.5 h. A solution of 0.86 g (2.85 mmol) of triene (+)-**4b** in 5 mL of THF was added over a 10-min period. The resultant mixture was stirred at 0 °C for 1 h and at room temperature for 11 h. After cooling to 0 °C the reaction was treated with 5.8 mL of water, 22.4 mL of 40% sodium hydroxide, and 18.1 mL of 30% hydrogen peroxide. The mixture was warmed to room temperature and stirred for 18 h. The aqueous layer was saturated with sodium chloride, the organic layer was separated, and the aqueous layer was diluted with water until homogeneous and extracted with ether. The combined organic layers were washed with brine and dried over magnesium sulfate. Removal of solvents at reduced pressure afforded 0.855 g (89%) of (+)-**5b** as a viscous oil: IR (film) ν 3300, 2900, 2750, 1460, 1440, 1070, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0–2.0 (m), 2.1–2.6 (m), 3.1 (br s, OH), 3.55 (t, CH_2–O–); ^{13}C NMR ($CDCl_3$) δ 133.9, 62.9, 32.8, 31.7, 29.5, 29.1, 26.1, 25.7, 25.6, 24.9, 24.7; $[\alpha]^{28}_D$ +30.3° (*c* 3.00, $CHCl_3$).

(*R*)-(+)-1,2-Bis(4-formylbutyl)cyclododecene (6). To a cooled (0 °C) stirred slurry of 2.06 g (9.53 mmol) of pyridinium chlorochromate[38] and 2 g of Celite (oven-dried) in 20 mL of dichloromethane was added dropwise a solution of 0.805 g (2.38 mmol) of diol (+)-**5** in 5 mL of dichloromethane. The reaction mixture was allowed to warm to room temperature and stirred for 4 h. The resultant slurry was diluted with ether and filtered through Florisil with the aid of ether. Removal of solvents at reduced pressure afforded 0.654 g (82%) of (*R*)-(+)-**6** as a pale yellow oil which was used without further purification: IR (film) ν 2910, 2850, 2705, 1730, 1475, 1420, 1395, 1370, 1360, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0–2.0 (m), 2.15–2.7 (m), 9.73 (s, CHO); ^{13}C NMR ($CDCl_3$) δ 202.3, 133.8, 43.7, 31.4, 29.4, 28.8, 26.0, 25.6, 24.8, 24.6, 21.9; $[\alpha]^{28}_D$ +77.1° (*c* 2.62, $CHCl_3$).

(*R*)-(+)-[10.10]Betweenanene (8). The modified McMurry procedure[23] developed by T. H. Black[39] was followed exactly by using 5 g of titanium trichloride and 10.5 cm (64.9 mmol) of lithium wire (cut into 2–3 mm pieces) in 60 mL of DME. This stirred slurry was heated to reflux under argon for 2 h to give a jet-black solution with brown foam. A solution of 500 mg (1.50 mmol) of dialdehyde (+)-**6** in 45 mL of DME was then added over a 16-h period via syringe pump. Reflux was continued for an additional 3 h. Addition of 10 g of Celite to the cooled black reaction mixture gave a slurry which was filtered through a pad of Celite with the aid of hexane. Removal of solvents at reduced pressure gave a residue which was taken up in hexane and filtered with hexane on a column containing silica gel topped with a pad of Florisil. Removal of solvent from the elutant gave 251 mg (56%) of a clear, colorless oil. GC analysis showed a trace of hydrocarbon impurity. The oil was chromatographed (silica gel, hexane) to give 198 mg (44%) of dienes (+)-**7** as a clear, colorless oil which contained two closely separated products by GC analysis (cis/trans isomers): IR (film) ν 2925, 2850, 1480, 975 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0–1.65 (m), 1.65–2.15 (m), 2.15–3.65 (m), 5.3 (m, C=C—H, cis isomer), 5.45 (m, C=C—H, trans isomer); $[\alpha]^{29}_D$ +74.8° (*c* 2.96, $CHCl_3$).

A slurry of 50 mg of platinum on carbon in 15 mL of ethyl acetate was equilibrated under a hydrogen atmosphere. To this vigorously stirred mixture was added 198 mg (0.66 mmol) of dienes **7** in 5 mL of ethyl acetate. After 5 h the reaction mixture was filtered through Celite with the aid of hexane. Removal of solvent at reduced pressure gave 190 mg (95%) of (+)-**8** as a white, waxy solid, mp 85–88 °C (crystal change 79–83 °C), which was recrystallized from cold hexane to give waxy needles, mp 87–90 °C: IR ($CDCl_3$) ν 2925, 2850, 1475, 1450, 1350, 1275, 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0–1.7 (m, 32 H), 2.1 (m, 4 H), 2.25–2.75 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 135.0, 31.0, 26.6, 26.5, 24.6, 24.4; $[\alpha]^{29}_D$ +46.9° (*c* 1.16, $CHCl_3$); GC–MS M^+ 304. Anal. Calcd for $C_{22}H_{40}$: C, 88.76; H, 13.24. Found: C, 86.84, H, 13.35.

(1*S*,2*S*)-(−)-1,2-Dipentylcyclododecane-1,2-diol (11). To a stirred solution of 0.150 g (0.49 mmol) of olefin (+)-**4a** in 2 mL of pyridine was added 0.310 g (1.22 mmol) of osmium tetroxide. TLC analysis showed no reaction had taken place after 5 h. Therefore, an additional 0.313 g (1.23 mmol) of osmium tetroxide was added. After 18 h, TLC again showed no reaction so 0.300 g (1.18 mmol) of osium tetroxide and 0.111 g (1.0 mmol) of trimethylamine *N*-oxide dihydrate were added and stirring was continued for 7.5 h during which the starting olefin was consumed. The reaction was quenched with 1.25 g of sodium bisulfite in 8 mL of pyridine and 15 mL of water, stirred for 30 min, poured into water, and extracted with ether. The combined organic layers were washed with 10% hydrochloric acid, water, and brine and dried over magnesium sulfate. Removal of solvent gave 174 mg of a crude dark oil which was chromatographed (silica gel, 10% ethyl acetate–hexane) to give two fractions:

Fraction 1: R_f 0.30 (10% ethyl acetate–hexane); 23 mg of star needles; mp 86–87 °C; ^{13}C NMR ($CDCl_3$) δ 211.5, 42.7, 31.4, 29.3, 29.2, 23.85, 23.55, 22.4, 13.85. The ^{13}C NMR spectrum was identical with that obtained by Black for docosane-6,17-dione.[41]

Fraction 2: R_f 0.47 (10% ethyl acetate–hexane); 141 mg of a purple-black thick oil presumed to be the osmic ester of diol **11**.

Fraction 2 was carried on following the procedure of Castells.[30] To a stirred slurry of 0.50 g (13.25 mmol) of lithium aluminum hydride in 2 mL of THF was added fraction 2 as a solution in 11 mL of THF. This mixture was heated to reflux for 12 h, cooled to 0 °C, quenched with 0.5 mL of water, 0.5 mL of 10% sodium hydroxide, and 1.5 mL of water, and stirred for 45 min. This slurry was filtered by suction through a pad of Celite and magnesium sulfate with the aid of ether. Removal of solvents gave 86 mg (51%) of solid diol (−)-**11**. Purification by chromatography (silica gel, 10% ethyl acetate–hexane) gave 66 mg (40%) of (1*S*,2*S*)-(−)-diol **11**: mp 75–77 °C; IR ($CHCl_3$) ν 3300, 2900, 2850, 1475 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9 (t, J = 6 Hz), 1.1–1.7 (m), 1.7 (br s); ^{13}C NMR ($CDCl_3$) δ 79.55, 34.4, 32.7, 32.2, 26.2, 24.9, 23.4, 22.7, 21.3, 20.8, 14.0; $[\alpha]^{27}_D$ −45.7° (*c* 2.0, $CHCl_3$).

(±)-1,2-Dipentylcyclododecane-1,2-diol (11). To a stirred solution of 1.43 g (4.67 mmol) of olefin (±)-**4a** and 1.14 g (10.28 mmol) of trimethylamine *N*-oxide in 30 mL of ether was added, dropwise, a solution of 1.31 g (5.14 mmol) of osmium tetroxide in 20 mL of ether. The reaction mixture was heated to reflux for 30 min to give an olive-green-black solution. The cooled mixture was poured into water and extracted with ether. The combined ethereal layers were washed with ice-cold 10% hydrochloric acid, water, and brine and dried over anhydrous magnesium sulfate. Removal of solvents gave 2.19 g of a crude black syrup which was immediately taken on without further purification.

To a stirred, cooled (0 °C) slurry of 10.34 g (0.272 mol) of lithium aluminum hydride in 125 mL of THF was added a solution of 2.19 g of the crude osmic ester in 25 mL of THE. The mixture was heated to reflux for 1 h, cooled to 0 °C, quenched with 10.4 mL of water, 10.4 mL of 10% sodium hydroxide, and 31.2 mL of water, and stirred for 30 min. The slurry was filtered with suction through a pad of Celite and magnesium sulfate with the aid of ether. Removal of solvents gave a crude solid which was chromatographed (silica gel, 10% ethyl acetate–hexane) to give 0.987 g (62%) of diol (±)-**11** as a white, crystalline solid, mp 104–105.5 °C: IR ($CHCl_3$) ν 3300, 2900, 2850, 1475 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9 (t, J = 6 Hz), 1.1–1.7 (m), 1.7 (br s); ^{13}C NMR ($CDCl_3$) δ 79.6, 34.5, 32.8, 32.3, 26.3, 25.0, 23.5, 22.8, 21.4, 20.9, 14.1. Anal. Calcd for $C_{22}H_{44}O_2$: C, 77.58; H, 13.02. Found: C, 77.85; H, 12.79.

(*S*)-(+)-(*Z*)-1-Formyl-2-pentylcyclododecene (12a). To a stirred slurry of 1.42 g (12.5 mmol) of manganese dioxide in 7 mL of benzene was added a solution of 0.20 g (0.75 mmol) of alcohol (+)-**2a** in 8 mL of benzene. The reaction was stirred vigorously for 2 h then filtered through a pad of Celite with the aid of hexane. Removal of solvents gave 0.198 g (100%) of aldehyde (+)-**12a** as a viscous clear oil: IR (film) ν 2900, 2850, 1670, 1630, 1470, 1450, 1150 cm^{-1}; ^1H NMR 80 MHz ($CDCl_3$) δ 0.8 (t, CH_3CH_2, J = 8 Hz), 0.95–1.6 (m), 1.7–2.2 (m), 2.2–2.7 (m), 2.8–3.3 (m), 9.95 ppm (s, CHO); ^{13}C NMR ($CDCl_3$) δ 191.5, 164.0, 137.8, 35.6, 31.9, 28.8, 28.2, 27.5, 26.5, 26.4, 26.3, 23.8, 23.7, 23.4, 23.3, 22.4, 13.8; $[\alpha]^{22}_D$ +103.6° (*c* 1.42, $CDCl_3$).

(*S*)-(+)-(*Z*)-1-Formyl-2-(11-dodecenyl)cyclododecene (12c). The procedure described for (+)-**12a** using 1.72 g (4.75 mmol) of (+)-**2c** ($[\alpha]_D$ +47.8°, 99% ee) and 9 g (79 mmol) of manganese dioxide in 100

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(41) Van Rheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973–6.

mL of benzene afforded 1.57 g (92%) of (*R*)-(+)-aldehyde **12c** as a clear, viscous oil: IR (film) ν 2900, 2840, 1665, 1640, 1470, 920 cm^{-1}; ^{1}H NMR 60 MHz ($CDCl_3$) δ 1.0–1.75 (m), 1.8–2.3 (m), 2.3–3.4 (m), 4.95 (m, CH=CH_2), 5.75 (m, CH=CH_2), 10.05 (s, CHO); ^{13}C NMR ($CDCl_3$) δ 191.3, 163.7, 138.9, 137.8, 114.0, 35.6, 33.6, 29.7, 29.4, 29.0, 28.8, 28.5, 27.5, 26.5, 26.4, 26.3, 23.8, 23.7, 23.4, 23.4; $[\alpha]^{20}_D$ +97.9° (*c* 1.87, $CHCl_3$).

(*S*)-(+)-(*Z*)-1-(1-Hydroxypentyl)-2-pentylcyclododecene (13a). To a stirred solution of 0.198 g (0.75 mmol) of aldehyde (+)-**12a** in 0.9 mL of ether was added 0.82 mL (0.90 mmol) of 1.1 M *n*-butylmagnesium bromide in THF. After 30 min the mixture was poured into 10% hydrochloric acid and extracted with ether. The combined ethereal layers were washed with saturated sodium bicarbonate and brine and dried over anhydrous potassium carbonate. Removal of solvents gave 0.24 g of a crude oil which was chromatographed (silica gel, 10% ethyl acetate–hexane) to yield 0.145 g (60%) of alcohol **13a** as a clear, colorless oil: IR (film) ν 3350, 2900, 2840, 1465 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.85 (t, J = 6 Hz, CH_3CH$_2$), 1.0–1.7 (m), 1.7–2.65 (m), 4.65 (m); ^{13}C NMR ($CDCl_3$) δ 136.0, 135.9, 72.1, 37.7, 33.1, 31.9, 28.8, 28.0, 27.9, 27.2, 26.5, 26.2, 24.9, 24.4, 24.1, 24.0, 23.9, 22.7, 22.65, 14.0; $[\alpha]^{20}_D$ +32.0° (*c* 0.89, $CHCl_3$).

(*S*)-(+)-(*Z*)-1-(1-Hydroxy-11-dodecenyl)-2-(11-dodecenyl)cyclododecene (13c). The procedure described for (+)-**13a** was followed by using 1.57 g (4.36 mmol) of aldehyde (+)-**2c**, 8.72 mL (5.23 mmol) of 0.6 M undecenylmagnesium bromide in THF, and 5 mL of ether. After workup and chromatography (silica gel, 10% ethyl acetate–hexane) 1.86 g (83%) of alcohol (+)-**13c** was isolated as a mobile, clear oil: IR (film) ν 3400, 3050, 2900, 2800, 1620, 1450, 900 cm^{-1}; ^{1}H NMR 60 MHz ($CDCl_3$) δ 1.0–1.8 (m), 1.8–2.7 (m), 4.7 (br t, CH–OH), 4.9 (m, CH=CH_2), 5.7 ppm (m, CH=CH_2); ^{13}C NMR ($CDCl_3$) δ 139.1, 136.0, 135.8, 114.0, 72.1, 38.0, 33.8, 33.2, 29.7, 29.63, 29.60, 29.5, 29.1, 28.9, 28.8, 27.9, 27.2, 26.5, 26.25, 25.8, 25.0, 24.4, 24.1, 24.0, 23.9; $[\alpha]^{20}_D$ +23° (*c* 5.13, $CHCl_3$).

(*S*)-(+)-(*Z*)-1-(1-Acetoxypentyl)-2-pentylcyclododecene (14a). To a stirred, cooled (0 °C) solution of 0.145 g (0.45 mmol) of alcohol (+)-**13a** and 0.065 g (0.54 mmol) of 4-(dimethylamino)pyridine in 3.5 mL of pyridine was added 0.13 mL (1.41 mmol) of acetic ahydride. After 2 h at 0 °C the reaction was quenched with methanol, poured into water, and extracted with ether. The combined organic layers were washed with ice-cold 5% hydrochloric acid (until the washes were acidic), saturated sodium bicarbonate, and brine and dried over anhydrous potassium carbonate. Removal of solvents gave 163 mg (99%) of acetate (+)-**14a** as a clear, colorless oil which was used immediately without further purification: IR (film) ν 2900, 2850, 1740, 1470, 1380, 1240, 1020 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.85, 0.82 (two triplets, J = 5 Hz, CH_3CH$_2$), 1.0–1.8 (m), 1.8–2.7 (m), 2.0 (s, $COCH_3$), 5.98 (t, J = 6 Hz, CHOAc); ^{13}C NMR ($CDCl_3$) δ 170.1, 139.0, 131.8, 74.1, 34.5, 33.1, 31.9, 29.4, 28.6, 27.4, 27.3, 26.9, 26.3, 26.0, 25.5, 24.4, 24.0, 23.8, 22.6, 22.5, 21.3, 13.9, 13.85; $[\alpha]^{20}_D$ +30.2° (*c* 1.19, $CHCl_3$).

(*S*)-(+)-(*Z*)-1-(1-Acetoxy-11-dodecenyl)-2-(11-dodecenyl)cyclododecene (14c). The procedure described for (+)-**14a** was followed by using 1.86 g (3.62 mol) of alcohol (+)-**13c**, 0.522 g (3.55 mmol) of 4-(dimethylamino)pyridine, and 1.0 mL (11.41 mmol) of acetic anhydride in 25 mL of pyridine. After workup, removal of solvents afforded 2.0 g (99%) of (*R*)-(+)-acetate **14c** as a colorless, viscous oil: IR (film) ν 2900, 2800, 1715, 1630, 1460, 1240, 900 cm^{-1}; ^{1}H NMR 60 MHz ($CDCl_3$) δ 0.9–1.7 (m), 1.7–2.7 (m), 2.0 (s, $COCH_3$), 4.9 (m, C=CH_2), 5.7 (m, CH=CH_2), 5.9 (br t, J = 6 Hz, CHOAc); ^{13}C NMR ($CDCl_3$) δ 169.8, 138.9, 138.8, 131.85, 114.0, 73.9, 34.9, 33.7, 33.1, 29.6, 29.54, 29.46, 29.4, 29.0, 28.8, 27.2, 26.9, 26.2, 25.9, 25.5, 25.2, 24.4, 24.0, 23.8, 21.1; $[\alpha]^{20}_D$ +27.2° (*c* 6.06, $CHCl_3$).

(*S*)-(*E*)-1-(1-Acetoxy-11,12-dihydroxydodecyl)-2-(11,12-dihydroxydodecyl)cyclododecene (15). The procedure of Van Rheenen was followed.[41] To a stirred, cooled (0 °C) solution of 1.61 g (14.48 mmol) of trimethylamine *N*-oxide, 18.1 mL (0.362 mmol) of 0.02 M osmium tetroxide in *tert*-butyl alcohol, and 3 mL of water was added dropwise 2.0 g of acetate (+)-**14c** in 3 mL of acetone. After 12 h, the mixture was poured into a solution of 1.15 g of sodium metabisulfite in 90 mL of water. The resultant solution (pH 8) was cooled to 0 °C and acidified with ice-cold 5% hydrochloric acid to pH 2. This solution was saturated with sodium chloride and extracted with ethyl acetate. The combined organic layers were washed with ice-cold 5% hydrochloric acid, saturated sodium carbonate, and brine and dried over anhydrous potassium carbonate. Removal of solvents gave 2.23 g (99%) of (*R*)-tetraol **15** as a brown syrup: IR (film) ν 3300, 2900, 2825, 1720, 1460, 1230, 1080, 1040, 1020 cm^{-1}; ^{1}H NMR 60 MHz ($CDCl_3$) δ 1.0–1.8 (m), 1.8–2.7 (m), 2.0 (s, $COCH_3$), 3.25–2.7 (m), 4.0–4.3 (m), 5.9 ppm (br t, CHOAc).

(*R*)-(+)-(*E*)-1,2-Bis(11,12-dihydroxydodecyl)cyclododecene (16). The procedure employed for the synthesis of (+)-**4a** was followed by using 2.23 g (3.57 mmol) of acetate (+)-**15**, 1.14 g (0.162 g-atom) of lithium wire, 100 mL of ethylamine, and 15 mL of THF. Workup and removal of solvents gave 2.1 g of tetraol (+)-**16** as a viscous syrup: IR (film) ν 3300, 2900, 2850, 1460, 1070 cm^{-1}; ^{1}H NMR 60 MHz ($CDCl_3$) δ 1.0–1.8 (m), 1.8–2.7 (m), 2.0 (s, $COCH_3$), 3.25–3.7 (m), 4.2 (br s, OH); ^{13}C NMR ($CDCl_3$) δ 133.65, 72.1, 66.4, 34.5, 32.9, 31.6, 29.4, 29.35, 29.2, 25.9, 25.5, 24.7, 24.5, 20.7, 18.7, 13.9, 13.6; $[\alpha]^{20}_D$ +18.4° (*c* 6.22, $CHCl_3$); HRMS calcd for $C_{36}H_{70}O_4$, 566.5274; found, 566.5301.

(*R*)-(+)-(*E*)-1,2-Bis(10-formyldecyl)cyclododecene (17). To a stirred solution of 2.1 g (3.57 mmol) of tetraol (+)-**16** in 100 mL of dioxane and 40 mL of water was added 1.69 g (7.91 mmol) of sodium metaperiodate in small portions. After 16 h, the reaction was poured into water and extracted with ethyl acetate and with ether. The combined organic layers were washed with water and brine and dried over anhydrous magnesium sulfate. Removal of solvents gave 1.46 g of yellow oil which was taken up in 80 mL of ether and washed again with water and brine and dried over magnesium sulfate. Removal of solvents gave 1.23 g (69%) of dialdehyde (+)-**17** as a clear, mobile oil: IR (film) ν 2925, 2850, 1730, 1460 cm^{-1}; ^{1}H NMR 60 MHz ($CDCl_3$) δ 1.0–1.9 (m), 2.0–2.6 (m), 9.68 (t, J = 2 Hz, CHO); ^{13}C NMR ($CDCl_3$) δ 202.1, 133.7, 43.6, 31.6, 29.4, 29.2, 28.95, 25.95, 25.55, 24.8 24.6, 21.6; $[\alpha]^{20}_D$ +20.8° (*c* 3.22, $CHCl_3$).

(*R*)-(+)-[22.10]Betweenanene (19). The procedure described for diene **7** was employed by using 0.600 g (1.2 mmol) of dialdehyde (+)-**17**, 0.448 g (64.9 mmol) of lithium wire, 5 g of titanium trichloride, and 100 mL of DME. Workup afforded 0.313 g (56%) of diene **18** as a clear, colorless oil: IR (film) ν 2900, 2850, 1460, 980 cm^{-1}; ^{1}H NMR 60 MHz ($CDCl_3$) δ 1.0–1.7 (m), 1.7–2.1 (m), 2.1–2.5 (m), 5.2 ppm (m, C=C—H); ^{13}C NMR ($CDCl_3$) δ 134.1, 130.6, 32.0, 31.9, 31.4, 29.9, 29.8, 29.6, 29.4, 29.25, 29.2, 29.0, 28.9, 28.6, 27.8, 26.2, 25.9, 25.0, 24.8, 22.7, 14.1.

This sample of diene **18** was hydrogenated over 70 mg of platinum-on-carbon in 25 mL of ethyl acetate. Filtration and removal of solvent gave 290 mg (92%) of a viscous oil which was chromatographed on 10% silver nitrate–silica gel using hexane as the eluant: IR (film) ν 2900, 2850, 1460 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.1–1.6 (m), 1.6–2.0 (m), 2.2–2.6 (m); ^{13}C NMR (CD_2Cl_2) δ 134.6, 32.2, 30.2, 30.1, 29.9, 29.74, 29.7, 29.5, 29.3, 29.0, 28.9, 28.5, 28.3, 26.7, 26.4, 25.6, 25.3; $[\alpha]_D$ +27.2° (*c* 1.93, $CHCl_3$); GC–MS: M^+ 472.6. Co-injection with racemic [22.10]betweenanene under conditions found to separate the cis isomer gave a single peak. Anal. Calcd for $C_{34}H_{64}$: C, 86.36; H, 13.64. Found: C, 86.42; H, 13.82.

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