heterogeneous hydroquinone–benzoquinone electrode is reversible and its potential can be varied by altering the pH, we thought that homogeneous systems involving this couple might show similar behavior. However, we were unable to find any redox reaction involving this couple[14] in which reactants were converted essentially completely to products and then regenerated by changing the pH.

In one of the most thorough studies of the kinetics of the benzoquinone–hydroquinone redox system,[14d] Castro and coworkers examined the oxidation of hydroquinone by low-spin iron(III) porphyrins and the reduction of benzoquinone by low-spin iron(II) prophyrins. Redox reactions were shown to proceed in both directions, but only initial rates could be used because pseudo-order plots drifted with time. Because of the nonideal behavior, a complete kinetic analysis could not be carried out and no attempt to completely shift an equilibrium mixture could be made.

Likewise, redox indicators and dyes are other systems which come to mind when organic molecules which may undergo reversible redox reactions are being screened. However, these systems are not completely reversible as they have a tendency to undergo slow irreversible solvolytic and photolytic decomposition.

From these results on thioether–sulfoxide interconversions it is clear that suitable neighboring groups effectively catalyze both the oxidation and the reduction reaction. These intramolecular catalysts can provide an efficient, reversible low-energy path for *electron-transfer, oxide-transfer, and proton-transfer processes* in biology. There is precedent for the suggestion that a thioether–sulfoxide couple may be important in biological redox reactions.[15] It has been proposed at various times that the conversion of a thioether to a sulfoxide could provide a molecular basis of oxidative phosphorylation.[12,15,16] However, Wang pointed out that sulfoxide reduction must also be achieved in an efficient way in order for the mechanism to be valid.[17]

Our results show that a thioether–sulfoxide two-electron interconversion is kinetically feasible when an intramolecular interaction leads to a stabilized cationic thioether intermediate.[18] Various other substituents on amino acid side chains may also be capable of providing anchimeric assistance.

Acknowledgment. We wish to thank the National Science Foundation for support of this research. We also thank J. H. Swinehart, P. A. Rock, and A. S. Hirschon for helpful discussions.

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(17) Wang, J. H. *J. Bioenerg.* **1976**, *8*, 209.
(18) Because thioether cation radicals are also well-known, one-electron, oxidations may also be catalyzed. In this regard it should be noted that an S–S bonded dimethionyl cation radical has been implicated as the source of the EPR signal on oxidation of yeast cytochrome *c* oxidase by hydrogen peroxide.[19]
(19) Hoffman, B. M.; Roberts, J. E.; Brown, T. G.; Kang, C. H.; Margoliash, E. *Proc. Natl. Acad. Sci. U.S.A.* **1979**, *76*, 6132.

Synthesis and Complexation Properties of Macrocyclic Polyethers Derived from Chiral and *meso*-1,1′-Bicyclohexyl-2,2′-diols[1,2]

Thomas W. Bell[3]

Contribution from the Department of Chemistry, University of California at Los Angeles, Los Angeles, California 90024. *Received August 11, 1980*

Abstract: Five novel macrocyclic polyether ligand systems containing the bicyclohexyl structural unit are reported. The requisite 1,1′-bicyclohexyl-2,2′-diols were prepared by hydroboration–oxidation of bi-1-cyclohexen-1-yls. Equimolar reaction of bi-1-cyclohexen-1-yl (**4**) with borane in THF, followed by oxidation, gave two products, *d,l*- and *meso-trans,trans*-[1,1′-bicyclohexyl]-2,2′-diols (**5** and **6**, 3:1, respectively). Employment of a larger excess of borane led selectively to diol **5**, which could be obtained in optically active form by using the novel resolving agent (–)-menthoxyacetaldehyde or by asymmetric hydroboration of **4**, using monoisopinocampheylborane. Hydroboration–oxidation of (3*R*,3′*R*,5*R*,5′*R*)-tetramethylbi-1-cyclohexen-1-yl, prepared in six steps from (+)-pulegone, gave a *pseudomeso*-1,4-diol (**14a**, 51%) and a symmetrical 1,4-diol (**15a**, 21%). Hydroboration–oxidation of 3,3,3′,3′,5,5,5′,5′-octamethylbi-1-cyclohexen-1-yl, prepared in three steps from isophorone, was controlled to yield a single product, *meso*-1,4-diol **14b**. Diols **5**, **6**, **14a**, **14b**, and **15a** were converted to the *trans–transoid–trans*-2,5,8,11,14,17-hexaoxatricyclo[22.4.0.0^{18,23}]octacosanes **24a** and **24b** and the trans–cisoid–trans analogues **25a**, **25b**, and **25c** by using sodium hydride and pentaethylene glycol ditosylate. The free energies of association of these systems in $CDCl_3$ at 25 °C with Li^+, Na^+, K^+, Rb^+, Cs^+, NH_4^+, $CH_3NH_3^+$, and *t*-$BuNH_3^+$ picrates and at 0 and 25 °C with *t*-$BuNH_3^+$ thiocyanate were determined. The ion selectivity of each bicyclohexyl ligand system was similar to those of analogous binaphthyl hosts and 18-crown-6 derivatives. The average negative free energies of association ($-\Delta G°_{av}$) for Li^+, Na^+, K^+, Rb^+, Cs^+, and NH_4^+ picrates decreased in the order **25a** > **24b** > **25b** = **24a** > **25c**. In the trans–transoid–trans series methylation (**24a** → **24b**) increased $-\Delta G°_{av}$, whereas in the trans–cisoid–trans series methylation (**25a** → **25b** → **25c**) decreased $-\Delta G°_{av}$.

The design of synthetic macrocyclic ligand systems capable of selective complexation with metal and ammonium cations has been the subject of numerous investigations.[4-7] The accurate prediction of complexation properties of such systems requires detailed knowledge of the structural factors that control molecular association. The ion and enantiomer selectivities of macrocyclic

(1) This work was supported by a grant from the National Science Foundation, CHE 77-00452, and was performed in the laboratories of Professor Donald J. Cram.
(2) Some of these synthetic results were outlined in a preliminary communication. Bell, T. W. *Tetrahedron Lett.* **1980**, 3443-3446.
(3) Current address: Cornell University, Department of Chemistry, Baker Laboratory, Ithaca, N.Y. 14853.

(4) (a) Chao, Y.; Weismann, G. R.; Sogah, G. D. Y.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 4948-4958 and earlier publications in this series. (b) Cram, D. J.; Cram, J. M. *Science* **1974**, *183*, 803-809. (c) *Acc. Chem. Res.* **1978**, *11*, 8-14.
(5) Lehn, J.-M. *Acc. Chem. Res.* **1978**, *11*, 49-57. *Pure Appl. Chem.* **1978**, *50*, 871-892.
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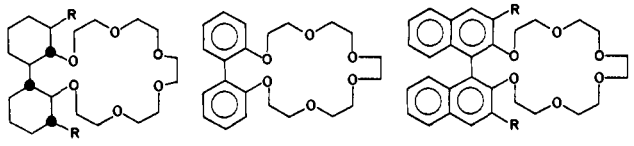
polyethers containing the 1,1′-binaphthyl structural unit have been particularly well explained through qualitative estimation of attractive and repulsive interactions.[4] According to this type of analysis, ligand conformations and relative orientations of host and guest are approximated by Corey–Pauling–Koltun (CPK) molecular models. Major repulsive forces are generally steric, whereas attractive forces are divided mainly into electrostatic (e.g., pole–dipole), hydrogen-bonding, and π–π[8] interactions.

Examination of CPK molecular models showed that the trans–transoid–trans[14] hexaoxatricycle **1a**, formally obtained by hydrogenation of cycle **2**,[9,10] could adopt a conformation closely resembling that of 1,1′-binaphthyl ligand **3** in complexes with alkylammonium salts.[4,8] In this conformation the best planes of the cyclohexane rings are noncoplanar, simulating the chiral barrier of the binaphthyl unit of **3**, which is enforced by hindered rotation about the 1,1′ bond. Furthermore, equatorial substituents (*R*), as in **1b**, extend this chiral barrier in a way that is spacially very similar to that in **3b**, which exhibits enhanced enantiomer selectivity for chiral alkylammonium ions.[8] It was also expected that aliphatic ligand **1** might display higher association constants toward alkaline metal and alkylammonium ions since two of the oxygen atoms of **3** are aryl substituted and should be accordingly less basic.[11] This effect might allow further extension of the chiral barrier of **1**, using far bulkier substituents than permitted in systems related to **3**.[12] In addition, cycle **1** possesses the desirable symmetry properties of **3**[13] and is fully saturated, eliminating the complication of π–π interactions between host and guest.[8] Reported here are the complexation properties of five trans–transoid–trans[14] and trans–cisoid–trans[14] macrocyclic polyethers related to **1**, as well as their syntheses via the corresponding [1,1′-bicyclohexyl]-2,2′-diols.[2]



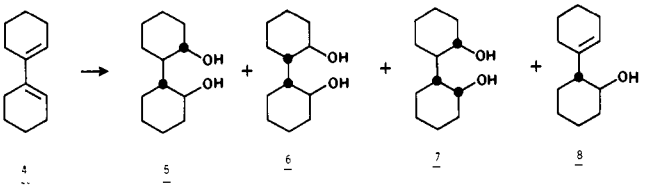
1 a) R = H
b) R = CH_3

2

3 a) R = H
b) R = CH_3

Results

Syntheses of the [1,1′-Bicyclohexyl]-2,2′-diols. In order to make macrocycle **1** available in large quantity, a short and efficient synthesis of *d,l-trans,trans*-[1,1′-bicyclohexyl]-2,2′-diol (**5**) was desired. The reaction of bi-1-cyclohexen-1-yl (**4**) with an equimolar amount of borane in tetrahydrofuran (BH_3–THF) at 0–20 °C, followed by oxidation with alkaline hydrogen peroxide, has been reported to yield the alcohol products **5–8** (58%, 5.8%, 3.4%, and 12%, respectively).[15] It was demonstrated that the unsaturated alcohol **8** resulted from incomplete hydroboration, rather than from dehydration of a 1,3-diol.[15] The small amount of *cis,trans*-diol **7** was probably due to partial inversion at carbon during the oxidation stage resulting from the presence of oxygen[16] rather than to trans borane addition to the double bond.[15]



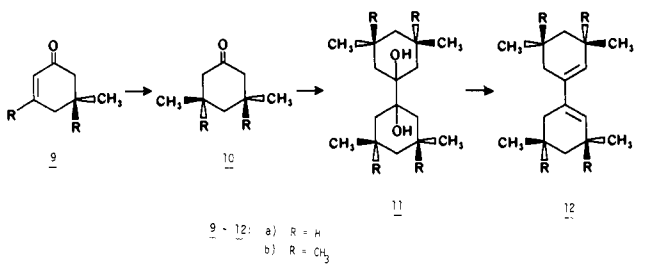
4 5 6 7 8

We have found that the reaction of BH_3–THF with **4** in 1.1:1 molar ratio at 0–65 °C, followed by oxidation as usual, produces a mixture consisting only of *d,l-trans,trans*-diol **5** and *meso-trans,trans*-diol **6** (3:1, respectively). In an effort to alter the product distribution, the reaction of diene **4** with thexylborane was also investigated.[16,17] Slow addition of equimolar thexylborane to diene **4** in THF, followed by heating the mixture under reflux for 21 h and oxidation, furnished a 3:1 mixture of **5** and **6** (89%) containing a small amount of unsaturated alcohol **8**. Employment of a 2:1 molar ratio of thexylborane to diene **4** led to complete reaction within 4.5 h, and a 9:2 mixture of **5** and **6** was produced (95%). This last result led to the use of a 2.1:1 molar ratio of BH_3–THF to diene **4** at about −20 to +20 °C. Oxidation as usual gave a crude product (98%) consisting of the desired diol **5**, accompanied by only a trace of diol **6**.

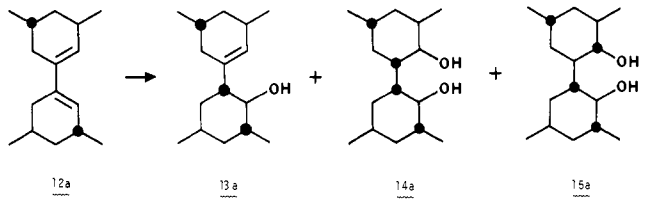
In order to avoid regiochemical problems in the synthesis of the diene precursors to macrocycles bearing equatorial methyl groups (e.g., **lb**),[18] efforts were directed toward the synthesis of bi-1-cyclohexen-1-yls with symmetrical substitution patterns. The cyclohexenones **9a,b** served as starting materials. The compound (*R*)-5-methyl-2-cyclohexen-1-one (**9a**) was prepared (79%) from (2*R*)-*trans*-2-bromo-5-methylcyclohexanone,[19] using magnesium oxide in *N,N*-dimethylformamide.[20] Multistep methods are reported to result in yields less than 65% for the same transformation.[19] Enone **9a** has also been prepared in 49% overall yield from (*R*)-3-methylcyclohexanone in three steps,[21] but the method reported here is considered more convenient for large-scale preparations. Conjugate addition of methylmagnesium bromide to **9a** and **9b** (isophorone) catalyzed by anhydrous cupric acetate led to (3*R*)-*trans*-3,5-dimethylcyclohexanone (**10a**, 77%) and 3,3,5,5-tetramethylcyclohexanone (**10b**, 93%), respectively, in better yields than those which were previously reported (**10a**, 70%;[19] **10b**, 82.5%[22] and 50%[23]). Ketone **10a** was reductively coupled using magnesium amalgam–titanium tetrachloride in THF[24] to afford pinacol **11a** (57%). Ketone **10b** was converted to pinacol **11b** (42%) using aluminum amalgam in dichloromethane,[25] a method more amenable to large-scale preparation. Finally, **11a** and **11b** were dehydrated by means of phosphorus oxychloride in pyridine[26,27] to give **12a** (98%) and **12b** (97%), respectively.

Reaction of chiral diene **12a** with excess BH_3–THF at −45 to −13 °C, followed by oxidation, gave three major products: unsaturated alcohol **13a** (40%), *pseudomeso*-diol **14a** (34%) and

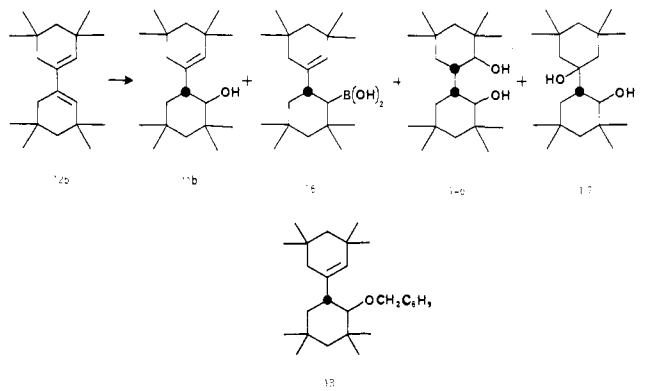
(8) See, for example: Peacock, S. C.; Domeier, L. A.; Gaeta, F. C. A.; Helgeson, R. C.; Timko, J. M.; Cram, D. J. *J. Am. Chem. Soc.* **1978**, *100*, 8190–8202.
(9) Izatt, R. M.; Christensen, J. J., Eds. "Synthetic Multidentate Macrocyclic Compounds"; Academic Press: New York, 1978; pp 9–11.
(10) Although the synthesis and catalytic hydrogenation of cycles similar to **2** have been mentioned by Pedersen,[9] the complexation properties of the products were not reported. This product would proabably be a mixture of cis–transoid–cis[14] and cis–cisoid–cis[14] isomers, as for the hydrogenation of dibenzo-18-crown-6: (a) Pedersen, C. J. *Org. Synth.* **1972**, *52*, 66. (b) Burden, I. J.; Coxon, A. C.; Stoddart, J. F.; Wheatley, C. M. *J. Chem. Soc., Perkin Trans. 1* **1977**, 220–226.
(11) Kamlet, M. J.; Solomonovici, A.; Taft, R. W. *J. Am. Chem. Soc.* **1979**, *101*, 3734–3739.
(12) Conversion of methyl groups to isopropyl groups in "dilocular" binaphthyl crown ethers seriously reduces their binding abilities.[8]
(13) Kyba, E. P.; Gokel, G. W.; de Jong, F.; Koga, K.; Sousa, L. R.; Siegel, M. G.; Kaplan, L.; Sogah, G. D. Y.; Cram, D. J. *J. Org. Chem.* **1977**, *42*, 4173–4184.
(14) This nomenclature conforms with IUPAC recommendations for tricyclic systems: *Pure Appl. Chem.* **1976**, *45*, 13–30.
(15) Plênat, F.; Pietrasanta, F.; Darvich, M. R.; Christol, H. *Bull. Soc. Chim. Fr.* **1976**, 2071–2074.
(16) Brown, H. C. "Organic Syntheses via Boranes"; Wiley: New York, 1975.
(17) Thexylborane has been shown to stereoselectively hydroborate dienes by a cyclic mechanism. E.g.: Brown, H. C.; Negishi, E. *J. Am. Chem. Soc.* **1967**, *89*, 5475–5478.
(18) Dehydration of the pinacol derived from (*R*)-3-methylcyclohexanone led to a mixture of three bi-1-cyclohexen-1-yls.
(19) Allinger, N. L.; Riew, C. K. *J. Org. Chem.* **1975**, *40*, 1316–1321.
(20) Miyano, M.; Dorn, C. R. *J. Org. Chem.* **1972**, *37*, 268–274.
(21) Oppolzer, W.; Petrzilka, M. *Helv. Chim. Acta* **1978**, *61*, 2755–2762.
(22) Kharasch, M. S.; Tawney, P. O. *J. Am. Chem. Soc.* **1941**, *63*, 2308–2315.
(23) Jefford, C. W.; McCreadie, R.; Muller, P.; Pfyffer, J. *J. Chem. Educ.* **1973**, *50*, 181–185.
(24) Corey, E. J.; Danheiser, R. L.; Chandrasekaran, S. *J. Org. Chem.* **1976**, *41*, 260–265.
(25) Schreibmann, A. A. P. *Tetrahedron Lett.* **1970**, *4271*–4272.
(26) Butenandt, A.; Schmidt-Thomé, J. *Ber. Dtsch. Chem. Ges.* **1938**, *71*, 1487–1492 *Ibid.* **1939**, *72*, 182–187.
(27) Greidinger, D. S.; Ginsburg, D. *J. Org. Chem.* **1957**, *22*, 1406–1410.



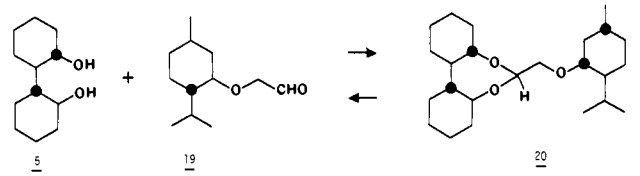
symmetrical diol **15a** (11%). When the hydroboration step was carried out at −40 to +2 °C, **14a** and **15a** were obtained in 51% and 21% yields, respectively. The ratio of these two diols was not significantly affected by further changes in reaction conditions. Furthermore, hydroboration–oxidation of the unsaturated alcohol **13a** also gave **14a** and **15a** in similar proportions.



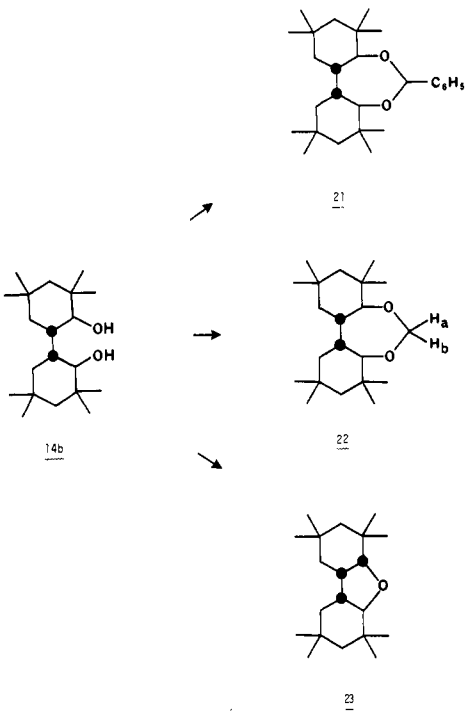
In the case of **12b**, hydroboration with BH_3–THF (1:2 molar ratio, 3–24 °C), followed by oxidation as usual, gave four major products, which were separated by chromatography: unsaturated alcohol **13b** (27%), borinic acid **16** (18%), *meso*-diol **14b** (14%) and 1,3-diol **17** (12%). None of the diastereomeric *d,l*-1,4-diol corresponding to **15a** could be detected. When the hydroboration reaction mixture was slowly warmed from −10 °C to ambient temperature and the oxidation step was prolonged, *meso*-diol **14b** was obtained as the sole product. Attempts were made to prepare a sample of the *d,l*-trans,trans diastereomer of **14b** by using unsaturated alcohol **13b**, which was conveniently prepared from BH_3–THF and **12b** (1.3:1 molar ratio) at −5 to +7 °C. Toward this end, benzyl ether **18** was hydroborated at −16 to +25 °C. After oxidation and removal of the benzyl group by hydrogenolysis, diol **14b** was obtained in 68% overall yield. Likewise, direct hydroboration–oxidation of **13b** (0–25 °C) afforded **14b** (91%).



Configurations of the [1,1′-Bicyclohexyl]-2,2′-diols. The relative configurations of the four asymmetric carbon atoms of *d,l*-diol **5** and *meso*-diol **6** had been established earlier by ^1H NMR spectroscopy and chemical correlation with *d,l*- and *meso*-[1,1′-bicyclohexyl]-2,2′-diones.[28] We report here corroborative evidence for this assignment through partial resolution of **5** using two independent methods. The first involved reaction of bi-1-cyclohexen-1-yl (**4**) with optically active monoisopinocampheylborane,[29,30] followed by oxidation and chromatography, affording diol **5** (42%, $[\alpha]^{25}_D$ +0.8° (*c* 1.60, $CHCl_3$)). The second method employed the novel resolving agent (−)-menthoxyacetaldehyde (**19**), which was most efficiently prepared (96%) by ozonolysis[31] of menthyl allyl ether.[32] Thus, acid-catalyzed condensation of diol **5** with chiral aldehyde **19** in the presence of molecular sieve powder[33] gave the solid acetal **20**, which was recrystallized to a constant melting point (mp 95.5–96.5 °C, $[\alpha]^{25}_D$ −53.7° (*c* 1.69, $CHCl_3$)). Hydrolysis liberated resolved diol **5** ($[\alpha]^{25}_D$ −3.1° (*c* 1.42, $CHCl_3$)). Unfortunately, the enantiomeric purity of optically enriched samples of **5** could not be determined by standard methods.[34]



The absolute configurations of diols **14a** and **15a** were inferred from their ^1H and ^{13}C NMR spectra, and complete enantiomeric purity was assumed.[35] The meso configuration of diol **14b** was suggested by its conversion to a mixture of diastereomeric acetals (**21**), though only one of the isomers could be isolated in a pure state. Definitive proof was secured by the presence of a low-field AB system in the ^1H NMR spectrum of formaldehyde acetal **22**, obtained by treatment of **14b** with *N*-bromosuccinimide in dimethyl sulfoxide.[36] An attempt to react **14b** with 2,2-dimethoxypropane and *p*-toluenesulfonic acid in benzene did not lead to a ketal, but formed the tetrahydrofuran derivative **23** instead (25%).[37]



Synthesis of the Macrocycles. The five [1,1′-bicyclohexyl]-2,2′-diols (**5**, **6**, **14a**, **14b**, and **15a**) were converted to the mac-

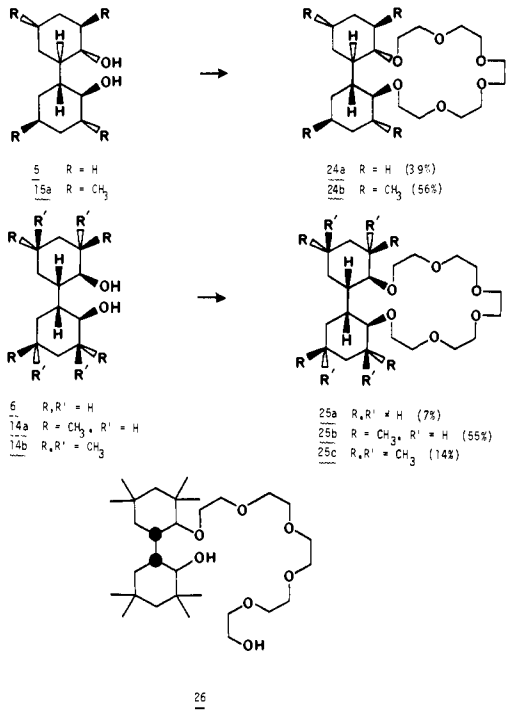
(28) Plĕnat, F.; Pietrasanta, F.; Darvich, M. R.; Christol, H. *Bull. Soc. Chim. Fr.* **1975**, *361*–365.
(29) Brown, H. C.; Yoon, N. M. *J. Am. Chem. Soc.* **1977**, *99*, 5514–5516.
(30) Brown, H. C.; Mandal, A. K. *Synthesis* **1978**, *146*–147.
(31) Pappas, J. J.; Keaveney, W. P.; Gancher, E.; Berger, M. *Tetrahedron Lett.* **1966**, 4273–4278.
(32) Corey, E. J.; Suggs, J. W. *J. Org. Chem.* **1973**, *38*, 3224.
(33) Roelofsen, D. P.; van Bekkum, H. *Synthesis* **1972**, *419*–420.
(34) The ^1H NMR signals of racemic **5** could not be resolved by use of chiral lanthanide shift reagents, and the diastereomers of acetal **20** could not be separated by gas–liquid phase chromatography (VPC) or by medium-pressure liquid (alumina and silica) chromatography.
(35) As in ref 19, epimerization of the intermediates should only introduce chemical impurities.
(36) Hanessian, S.; Y.-Chung, G.; Lavallee, P.; Pernet, A. G. *J. Am. Chem. Soc.* **1972**, *94*, 8929–8931. Hanessian, S.; Lavallee, P.; Pernet, A. G. *Carbohydr. Res.* **1973**, *26*, 258–260.
(37) The relative configuration of **23** was tentatively assigned as shown under the assumption that the relative configurations of the 1,1′-carbon atoms of **14b** were unchanged.

Table I. Equilibrium and Free Energy Parameters for Association between Macrocycles and *tert*-Butylammonium Thiocyanate in $CDCl_3$

macrocycle	24a	24b	25a	25b	3a[a]
$K_a \times 10^{-3}$ (M^{-1}) at 0 °C[b]	72	130	2000	290	37
$-\Delta G°$ (kcal/mol) at 0 °C[c]	6.1	6.4	7.9	6.8	5.7
$K_a \times 10^{-3}$ (M^{-1}) at 24 °C[b]	5.5	7.4	62	41	2.7
$-\Delta G°$ (kcal/mol) at 24 °C[c]	5.1	5.3	6.5	6.3	4.6

[a] Reference 44. [b] The method for determining K_a values has been described in ref 40. [c] $\Delta G°$ values are significant to about ±0.1 kcal/mol.

rocyclic polyethers (**24a**, **24b**, **25a**, **25b**, and **25c**) by reaction with sodium hydride and pentaethylene glycol ditosylate[38,39] in THF. Medium dilution conditions generally gave fair yields, except for two of the macrocycles. Much of **25a** was lost in mixed chromatographic fractions with minor side products, whereas **25c** was accompanied by the open-chain diol **26** (31%). All samples of hosts used in complexation experiments were rigorously purified by alumina and gel permeation chromatography.



Free Energies of Association between the Macrocycles and Metal and Ammonium Salts. A method involving extraction of *tert*-butylammonium thiocyanate from D_2O into a $CDCl_3$ solution containing the macrocyclic polyether was employed for the rapid screening of hosts for binding ability. According to a published procedure,[40] the ratio of *tert*-butylammonium ion to host was measured by ^1H NMR[41] and the association constant, K_a, and free energy of association, $\Delta G°$, were calculated. These parameters are defined by eq 1[42,43] and 2. The association parameters for

$$[M^+X^-] + [H] \overset{K_a}{\rightleftharpoons} [M^+ \cdot H \cdot X^-] \quad (1)$$

$$\Delta G° = -RT \ln K_a \quad (2)$$

Table II. Equilibrium and Free Energy Parameters for Association between Macrocycles and Alkali Metal, Ammonium, or Alkylammonium Picrates in $CDCl_3$ at 24 °C

host no.	M^+ of M^+ picrate$^-$	$K_a \times 10^{-3}$,[a] M^{-1}	$-\Delta G°$, kcal/mol	$-\Delta G°_{av}$,[b] kcal/mol	$-\Delta(\Delta G°)^{MeNH_3}_{t\text{-}BuNH_3}$,[c] kcal/mol
24a	Li	73	6.6	7.7	1.4
	Na	160	7.1		
	K	4800	9.1		
	Rb	1000	8.2		
	Cs	88	6.7		
	NH_4	1500	8.4		
	$MeNH_3$	52	6.4		
	t-$BuNH_3$	4.4	5.0		
24b	Li	120	6.9	8.5	2.5
	Na	680	7.9		
	K	16000	9.8		
	Rb	5900	9.2		
	Cs	740	8.0		
	NH_4	6900	9.3		
	$MeNH_3$	290	7.4		
	t-$BuNH_3$	3.9	4.9		
25a	Li	320	7.5	9.3	2.4
	Na	630	7.9		
	K	43000	10.4		
	Rb	32000	10.2		
	Cs	8300	9.4		
	NH_4	40000	10.3		
	$MeNH_3$	2200	8.6		
	t-$BuNH_3$	34	6.2		
25b	Li	11	5.5	7.7	1.7
	Na	81	6.7		
	K	14000	9.7		
	Rb	1900	8.5		
	Cs	160	7.1		
	NH_4	3100	8.8		
	$MeNH_3$	210	7.2		
	t-$BuNH_3$	12	5.5		
25c	Li	8	5.3	5.7	2.1
	Na	7	5.2		
	K	150	7.0		
	Rb	29	6.1		
	Cs	3	4.7		
	NH_4	32	6.1		
	$MeNH_3$	3.3	4.8		
	t-$BuNH_3$	0.1	2.7[d]		
3a[e]	Li	3.2	4.8	7.1	
	Na	100	6.8		
	K	1900	8.6		
	Cs	260	7.4		
	NH_4	740	8.0		
3b[e]	Li	23	6.0	8.5	0.7
	Na	1700	8.5		
	K	43000	10.4		
	Rb	4700	9.1		
	Cs	580	7.9		
	NH_4	3300	8.9		
	$MeNH_3$	170	7.1		
	t-$BuNH_3$	49	6.4		

[a] The method for determining K_a values has been described in ref 42. [b] Average of the $-\Delta G°$ values for association of each host with Li^+, Na^+, K^+, Rb^+, Cs^+, and NH_4^+, except for **3a**, where $-\Delta G°_{av}$ is the average of all values except that for Rb^+. [c] $\Delta G°_{t\text{-}BuNH_3} - \Delta G°_{MeNH_3}$. [d] This value is significant to only ±0.3 kcal/mol. [e] Reference 42.

hosts **24a**, **24b**, **25a**, and **25b** toward *tert*-butylammonium thiocyanate are given in Table I, in comparison with those for 1,1′-binaphthyl-20-crown-6 (**3a**).[44] Even using the most sensitive

(38) Kyba, E. P.; Helgeson, R. C.; Madan, K.; Gokel, G. W.; Tarnowski, T. L.; Moore, S. S.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 2564–2571.
(39) Newcomb, M.; Moore, S. S.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6405–6410.
(40) Timko, J. M.; Moore, S. S.; Walba, D. M.; Hiberty, P. C.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 4207–4219.
(41) It was assumed that the host concentration remained unchanged since all hosts reported here were insoluble in D_2O under the experimental conditions.
(42) Helgeson, R. C.; Weisman, G. R.; Toner, J. L.; Tarnowski, T. L.; Chao, Y.; Mayer, J. M.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 4928–4941.
(43) M^+, X^-, and H refer to guest cation, counterion, and macrocyclic host, respectively. All concentrations are in $CDCl_3$.
(44) Timko, J. M.; Helgeson, R. C.; Newcomb, M.; Gokel, G. W.; Cram, D. J. *J. Am. Chem. Soc.* **1974**, *96*, 7097–7099. K_a's corrected for revision of K_d for *tert*-butylammonium thiocyanate.[40]

procedure (scale C^{40}), too little *tert*-butylammonium salt was extracted by host **25c** to be detected by this method.

Association constants were also determined for the binding of alkali metal, ammonium, and alkylammonium picrates by macrocyclic ethers **24a**, **24b**, **25a**, **25b**, and **25c**. Following a published method,[42] aqueous solutions of Li^+, Na^+, K^+, Rb^+, Cs^+, NH_4^+, $MeNH_3^+$ (methylammonium), and t-$BuNH_3$ (*tert*-butylammonium) picrates were equilibrated with solutions of each host in $CDCl_3$ at 24 °C. The UV absorbances of the organic layers at 380 nm yielded association constants and free energies of association, as shown in Table II, in comparison with the corresponding values for **3a**[42] and **3b**.[42] According to an analysis of random error associated with this method,[42] free energy values larger than 5.0 kcal/mol are significant to ±0.1 kcal/mol, whereas other values are accurate only to ±0.2 kcal/mol, unless otherwise indicated. To facilitate comparison, two additional values are listed for each host contained in Table II: $\Delta G°_{av}$, the average free energy of association toward the six ions Li^+, Na^+, K^+, Rb^+, Cs^+, and NH_4^+, and $-\Delta(\Delta G°)_{t\text{-}BuNH_3}^{MeNH_3} = \Delta G°_{t\text{-}BuNH_3} - \Delta G°_{MeNH_3}$.

Discussion

The hydroboration results reported here are synthetically interesting since it is seen that the hydroboration–oxidation reactions of two bi-1-cyclohexen-1-yls (**4** and **12b**) can be controlled to yield only one product (**5** and **14b**, respectively) if careful attention is paid to stoichiometry and reaction conditions. Furthermore, the *direction* of interannular relative asymmetric induction is dependent upon the degree of diene substitution. Thus, incremental methylation of diene **4** (leading to **12a** and then **12b**) produces an incremental change in product selectivity from the *d,l-trans,trans*-1,4-diol series to the *meso-trans,trans*-1,4-diol series (pseudomeso in the case of **12a**). Conformational preferences of the intermediate diene–BH_3 monoadduct might account for these phenomena.[45]

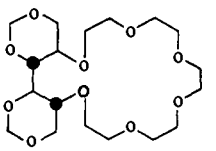
Several syntheses of chiral ligand systems have employed natural products as inexpensive sources of chirality, notably the sugars[7] and (−)-tartaric acid.[46] The syntheses of chiral hosts **24b** and **25b** utilize the terpene (+)-pulegone for this purpose. Moreover, these two hosts should be obtainable as either enantiomer since enone **9a** can easily be converted to (3*S*)-*trans*-3,5-dimethylcyclohexanone.[47-49]

The binding ability of hosts toward *tert*-butylammonium thiocyanate decreases in the following order: **25a** > **25b** > **24b** ~ **24a** > **3a** > **25c** (cf. Table I). The same order is seen for complexation of *tert*-butylammonium picrate (cf. Table II), except that the datum for **3a** is not available. This correlation suggests that the observed variation in binding ability is qualitatively dependent only on host–cation interactions and is not sensitive to counterion effects (at least for SCN^- and picrate$^-$).

It is observed (Table II) that the ion selectivity of each of the novel 20-crown-6 derivatives containing the 1,1′-bicyclohexyl-2,2′-diyl moiety (**24a,b**, **25a–c**) is similar to that exhibited by the binaphthyl crown ethers **3a,b** and also by derivatives of 18-crown-6.[42,50] In general, the best bound ion is potassium, followed by NH_4^+ or Rb^+. This suggests that the cavity size for each of these systems is roughly similar, as predicted by molecular model examination.

The $-\Delta G°_{av}$ value has been used to assess the overall binding ability of a host toward spherical (M^+) or near-spherical (NH_4^+) cations.[42,50,51] It is seen from Table II that the $-\Delta G°_{av}$ values decrease in the order **25a** > **24b** = **3b** > **25b** = **24a** ~ **3a** > **25c**. This variation does not seem to be strongly affected by hydrogen-bonding effects since the order of $-\Delta G°_{NH_4}$ values is roughly the same. The basicities of the oxygen ligands in these systems can be very roughly estimated by assuming that aromatization of a cyclohexane ring should reduce the basicity of an adjacent ether oxygen by a factor of 2.[52] According to this argument, the $-\Delta G°_{av}$ values for binaphthyl hosts **3a,b** should be only about five-sixths of those for bicyclohexyl systems **24a,b** and **25a–c**. The results bear no resemblance to this analysis, implying that inductive effects must be dominated by conformational and steric factors for these hosts. The $-\Delta(\Delta G°)_{t\text{-}BuNH_3}$ value is useful as a measure of the sensitivity of a host to the steric bulk of guests.[42,51] According to Table II, this parameter does not correlate in general with the degree of methylation of bicyclohexyl hosts, further suggesting the conformational dissimilarity of the complexes of these systems.

The optically active crown ether **27**, identical with host **24a** except for the replacement of four cyclohexane methylene groups by oxygen atoms, was recently reported.[53] However, **27** was found to be a much poorer binder of *tert*-butylammonium thiocyanate in $CDCl_3$ at 24 °C ($-\Delta G°$ = 3.7 kcal/mol).[53] This difference can be explained inductively if it is assumed that the 1,3-dioxan-2-yl oxygen ligands of **27** each suffer a two-thirds reduction in basicity (relative to **24a**), due to the presence of two anti-disposed oxygen atoms.[54] There may also be a conformational component of this discrepancy in free energies of association since the relative stabilities of the various rotational isomers about the interannular bond in each host may vary.[55]



27

Conformational models explaining the binding abilities of bicyclohexyl hosts **24a,b** and **25a–c** will be discussed in a later publication dealing with general conformational effects in crown ethers.

Experimental Section

General Procedure. All solvents were reagent grade. Tetrahydrofuran (THF) and pyridine were distilled from sodium benzophenone ketyl and calcium hydride, respectively. Dimethyl sulfoxide (Me_2SO) was decanted from CaH_2, and dimethylformamide (DMF) was distilled in vacuo and stored over 4-Å molecular sieves. Dichloromethane was fractionally distilled from CaH_2. Thin-layer chromatography (TLC) and preparative thick-layer chromatography plates were purchased from E. Merck. Adsorbents used for filtration and column chromatography were Woelm silica gel (silica) and neutral alumina. Medium-pressure chromatography was conducted on a 25 mm × 1000 mm Altex column packed with silica gel 60 (E. Merck, 40–63 μm) or Woelm alumina (neutral, 32–63 μm) at a pressure less than 120 psi and at a flow rate of 8–12 mL/min. Gel permeation chromatography was performed on a $^3/_8$ in. (o.d.) by 20 ft column packed with 200 g of 100-Å Styragel (Waters Associates, Inc.) with CH_2Cl_2 at a flow rate of 3.6–4.0 mL/min and a pressure of 400–900 psi. Gas–liquid phase chromatography (VPC) was carried out on a $^1/_8$ in. (o.d.) by 15 ft column of 5% Carbowax 20M on Anakrom A (90–100 mesh) at 137 °C, using a thermal conductivity detector. Melting points were measured on a Thomas-Hoover apparatus and are uncorrected. Mass spectra were recorded on an AEI MS-9 mass spectrometer at 70 eV, unless otherwise indicated. ^1H NMR spectra were recorded on a

(45) A possible mechanism of this type has already been mentioned.[2]
(46) Inter alia: Behr, J.-P.; Lehn, J.-M. *J. Chem. Soc., Chem. Commun.* **1978**, 143–146.
(47) Pak, C. S.; Djerassi, C. *Tetrahedron Lett.* **1978**, *4377*–4378.
(48) Burman, M. J. F.; Elliot, D. R.; Gordon, M. H.; Peck, R. G.; Robinson, M. J. T. *Tetrahedron Lett.* **1976**, 1535–1538.
(49) Goering, H. L.; Schmidt, W. W.; Singleton, V. D. *J. Org. Chem.* **1979**, *44*, 2282–2284.
(50) Helgeson, R. C.; Tarnowski, T. L.; Cram, D. J. *J. Org. Chem.* **1979**, *44*, 2538–2550.
(51) Koenig, K. E.; Lein, G. M.; Stuckler, P.; Kaneda, T.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 3553–3566.
(52) For the purpose of this crude estimation, it is assumed that the abilities of these ligands to stabilize cations (pole–dipole) is proportional to their hydrogen bond acceptor basicities, as suggested by the results for NH_4^+. The β values for diethyl ether, anisole, and diphenyl ether are 0.466, 0.223, and 0.128, respectively.[11]
(53) Laidler, D. A.; Stoddart, J. F. *Tetrahedron Lett.* **1979**, 453–456.
(54) A reduction in basicity of this order is reasonable since the basicity of tetrahydropyran (β = 0.544) is reduced by about one-third in passing to dioxane (β = 0.369).[11]
(55) These rotational isomers for **27** correspond to anti,anti conformers of 1,2-dimethoxyethane: Burkert, U. *Tetrahedron* **1979**, *35*, 1945–1951 and references cited therein.

Varian T-60 (60 MHz) or a Bruker WP-200 (200 MHz) spectrometer and ^{13}C NMR spectra were also recorded on a Bruker WP-200 (50.32 MHz) spectrometer. All chemical shifts are reported in ppm relative to internal $(CH_3)_4Si$. Infrared (IR) spectra were taken on a Perkin-Elmer Model 297 spectrophotometer, whereas electronic (UV) spectra were recorded on a Cary 14 or Beckman IR-4250 spectrometer, using diethyl ether as solvent. Optical rotations were measured on a Perkin-Elmer 141 polarimeter with a 1-dm thermostated cell. The procedures and instrumentation used for measurement of K_a values were exactly as described.[40,42]

Reagents and Starting Materials. Borane–tetrahydrofuran complex (BH_3–THF) was obtained as a 1.0 M solution in THF from Aldrich Chemical Co. Sodium hydride was used as a 50% dispersion in mineral oil, which was washed in the reaction flask with several portions of anhydrous pentane, hexane, or cyclohexane and then dried in a stream of N_2. Bi-1-cyclohexen-1-yl (**4**)[27] was obtained by dehydration of [1,1′-bicyclohexyl]-1,1′-diol,[24,56] which was prepared by reductive coupling of cyclohexanone, using aluminum amalgam in CH_2Cl_2.[25] (2*R*)-*trans*-2-Bromo-5-methyl-cyclohexanone,[19] mp 82.5–83 °C, $[\alpha]^{24.2}_{589}$ −63.5° (*c* 1.18, toluene), was prepared by bromination of (*R*)-3-methylcyclohexanone,[19,57] which was obtained from the acid-catalyzed hydration/retroaldol reaction of (+)-pulegone, $[\alpha]^{20}_{589}$ +22° (neat). Allyl menthyl ether[32] (bp 80–81 °C (4 mm)) was prepared by reaction of sodium menthoxide[58] with allyl bromide in toluene at 50 °C, followed by heating under reflux for 2 h. Pentaethylene glycol ditosylate[38,39] was prepared from pentaethylene glycol (bp 139–140 °C (0.02 mm); lit.[39] bp 173–174 °C (0.6 mm)), which was obtained by spinning-band distillation of commercial polyethylene glycol (average mol wt 200).

***d,l*- and *meso-trans,trans*-[1,1′-Bicyclohexyl]-2,2′-diols (5 and 6).** A solution of 7.07 g (43.6 mmol) of bi-1-cyclohexen-1-yl (**4**) in 44 mL of THF was stirred at 2–3 °C under N_2 as 48 mL of 1 M BH_3–THF was added dropwise over 70 min. The reaction mixture was stirred at 0–1 °C for 25 min, at 25 °C for 1 h, and under reflux for 10 min, then cooled to ambient temperature, and quenched by dropwise addition of 44 mL of ethanol. Aqueous NaOH (3 N, 26 mL) and 17.5 mL of 30% aqueous H_2O_2 were added dropwise, maintaining the internal temperature below 40 °C. The resulting mixture was stirred under N_2 at 46–56 °C for 1.25 h, cooled to ambient temperature, and saturated with K_2CO_3. The organic layer was extracted with saturated aqueous K_2CO_3 and dried (Na_2SO_4). Evaporation of the solvent gave 7.72 % (89%) of a white solid, whose ^1H NMR spectrum (60 MHz, Me_2SO-d_6) showed only the hydroxyl resonances of **5** and **6** (3:1, respectively, by integration). Chromatography on alumina with 100:0 to 92:8 (v/v) ether/methanol furnished two pure fractions: 3.42 g (40%) of **5**, mp 153–154.5 °C (lit.[15,28] mp 154 °C), and 0.82 g (9.5%) of **6**, mp 184 °C (lit.[15,28] mp 184 °C). The ^1H NMR data (60 MHz, Me_2SO-d_6) were identical with those reported for **5** and **6**.[15,28]

***d,l-trans,trans*-[1,1′-Bicyclohexyl]-2,2′-diol (5).** A solution of 15.4 g (95 mmol) of bi-1-cyclohexen-1-yl (**4**) in 140 mL of THF was stirred under N_2 at −25 to −21 °C as 200 mL of 1 M BH_3–THF was added dropwise over 1.5 h. The resulting clear solution was stirred at −25 to −15 °C for 1 h and then at −15 to −10 °C for 5.5 h and stored at 5 °C for 12 h. The reaction mixture was stirred at ambient temperature for 4 h and quenched by dropwise addition of 130 mL of ethanol. Aqueous NaOH (3 N, 150 mL) and 100 mL of 30% aqueous H_2O_2 were added dropwise, maintaining the internal temperature below 50 °C. The oxidation mixture was stirred under N_2 at 46–52 °C for 2 h, cooled to ambient temperature, and saturated with K_2CO_3, and the aqueous phase was extracted with two 100-mL portions of ether. The combined organic solutions were extracted with 50 mL of saturated aqueous K_2CO_3 and dried (K_2CO_3), and the solvents were removed at reduced pressure. The crude product consisted of 18.5 g (98%) of diol **5**, which was pure according to its ^1H NMR spectrum.[15,28] Recrystallization from benzene/hexane afforded 12.9 g (68%) of white needles, mp 152–153.5 °C.

(*R*)-5-Methyl-2-cyclohexen-1-one (9a). A suspension of 3.72 g (92.3 mmol) of magnesium oxide in 95 mL of DMF was stirred at 140 °C under N_2 as a solution of 13.7 g (71.6 mmol) of (2*R*)-*trans*-2-bromo-5-methylcyclohexanone in 25 mL of DMF was added dropwise over 8 min. The reaction mixture was stirred at 140 °C for 1 h, cooled to 0 °C, and quenched with 215 mL of cold 1.2 N aqueous HCl, added in portions. The resulting turbid yellow mixture was stirred at 0 °C until nearly transparent, diluted with 215 mL of cold water, and extracted with six 100-mL portions of ether. The combined extracts were washed with 100 mL each of water, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl and dried (Na_2SO_4). Distillation yielded 2.27 g (79%) of enone **9a** as a colorless mobile oil: bp 49–52 °C (3 mm) (lit.[19] bp (*d,l*) 54 °C (5 mm)); $[\alpha]^{25}_{589}$ −89.6° (*c* 0.89, $CHCl_3$) (lit.[19] $[\alpha]^{25}_{589}$ −90.17° (*c* 0.767, $CHCl_3$)). A chemical purity >98% was estimated by VPC.

(3*R*)-*trans*-3,5-Dimethylcyclohexanone (10a). A slurry consisting of 1.42 g (7.8 mmol) of anhydrous cupric acetate[59] and 27 mL of anhydrous ether was stirred at ambient temperature under N_2 as 27 mL of a 2.9 M solution of methylmagnesium bromide in ether was added in a continuous stream. The mixture was stirred for 0.5 h longer, cooled to −6 to −4 °C and stirred vigorously as a solution of 6.25 g (56.7 mmol) of enone **9a** in 57 mL of anhydrous ether was added dropwise over 40 min. The reaction mixture was stirred at 0 °C for 0.5 h and then at ambient temperature for 1 h, heated under reflux for 1 h, and quenched at 5–15 °C by dropwise addition of 39 mL of saturated aqueous NH_4Cl and 16 mL of 4 N aqueous HCl. The resulting mixture was stirred vigorously in air until the copper salts were completely dissolved; then the aqueous phase was extracted with three 25-mL portions of ether. The combined ether solutions were extracted with 15 mL of each of the following aqueous solutions: 1.2 N HCl, 10% $NaHCO_3$, and saturated NaCl. Drying (Na_2SO_4), followed by evaporation of the solvent and distillation of the residual light yellow oil gave 5.52 g (77%) of ketone **10a** as a colorless oil: bp 44–47 °C (2 mm) (lit.[19] bp (*d,l*) 36–37 °C (1.5 mm)); $[\alpha]^{25}_{589}$ −10.74° (*c* 1.145, $CHCl_3$) (lit.[19] $[\alpha]^{25}_{589}$ −12.28° (*c* 1.118, $CHCl_3$)); ^1H NMR (60 MHz, $CDCl_3$) δ 1.7–2.6 (m, ring, 8H), 1.00 (d, J = 7 Hz, CH_3, 6 H); IR (neat) 1704 cm^{-1}. VPC comparison with a commercial mixture of *cis*- and *trans*-3,5-dimethylcyclohexanones indicated the presence of only 3–5% of the cis isomer in the synthetic sample.

3,3,5,5-Tetramethylcyclohexanone (10b). A mixture of 36 g (0.2 mol) of anhydrous cupric acetate,[59] 2 mol of ethereal methylmagnesium bromide (2.9–3.0 M), and 500 mL of anhydrous ether was stirred at ambient temperature under N_2 for 0.5 h and then at 5–11 °C as a solution of 235 g (1.7 mol) of isophorone (**9b**) in 700 mL of anhydrous ether was added dropwise over 3 h. The dark reaction mixture was stirred under reflux for 4 h, allowed to stand at ambient temperature overnight, and then quenched by the addition of 1 L of saturated aqueous NH_4Cl, 300 mL of 1.2 N HCl, and 100 mL of concentrated hydrochloric acid. The resulting mixture was stirred vigorously in a stream of air until the copper salts dissolved. The deep blue aqueous layer was diluted with 100 mL of water and extracted with two 200-mL portions of ether. The combined ethereal solutions were extracted with saturated aqueous NH_4Cl, followed by water and saturated aqueous NaCl, and dried (Na_2SO_4). Solvent removal at reduced pressure, followed by fractional distillation, afforded 244.8 g (93%) of ketone **10b** as a colorless oil: bp 61–65 °C (4 mm) (lit. bp 59–61 °C (5.5 mm);[22] 79 °C (12 mm)[23]).

(3*R*,3′*R*,5*R*,5′*R*)-Tetramethyl-[1,1′-bicyclohexyl]-1,1′-diol (11a). According to the method of Corey,[24] a mixture of 0.44 g (1.66 mmol) of $HgCl_2$, 30 mL of THF, and 1.44 g (60 mmol) of magnesium powder (100 mesh) was stirred at ambient temperature under Ar for 15 min and the cloudy supernatant was withdrawn. The amalgam was washed with three 20-mL portions of THF and then stirred vigorously in 50 mL of THF at −10 to −4 °C as 3.3 mL (5.7 g, 30 mmol) of $TiCl_4$ was added dropwise over 5 min. The resulting suspension was stirred at −8 to −5 °C as a solution of ketone **10a** in 50 mL of THF was added dropwise over 5 min. After 45 min of stirring at 0–2 °C, the dark reaction mixture was quenched by dropwise addition of 5 mL of saturated aqueous K_2CO_3. The resulting brown mixture was stirred at 0–2 °C for 15 min, diluted with 150 mL of ether, and filtered through Celite, which was rinsed with 200 mL of ether. The combined filtrates were extracted with one 75-mL and two 50-mL portions of saturated aqueous NaCl, and these extracts were combined and extracted with 100 mL of ether and three 50-mL portions of pentane. All of the organic solutions were combined, dried (Na_2SO_4), and concentrated in vacuo, leaving a cloudy colorless oil, which was dissolved in ether. This solution was filtered and the solvent evaporated, affording 2.1 g of a clear oil, which solidified upon prolonged exposure to vacuum. Medium-pressure chromatography on alumina with 1:1 (v/v) ether/pentane, followed by pure ether, gave 1.47 g of diol **11a**, which was sublimed at 70 °C (1.2 mm), furnishing 1.44 g (56%) of crystalline solid: mp 69.5–70 °C; $[\alpha]^{25}_{589}$ +0.91°, $[\alpha]^{25}_{578}$ +0.89°, $[\alpha]^{25}_{546}$ +0.93°, $[\alpha]^{25}_{436}$ +0.74° (*c* 5.27, $CHCl_3$); M^+ *m/e* 254; ^1H NMR (200 MHz, $CDCl_3$) δ 0.898 (d, J = 6.59 Hz, CH_3, 6 H), 1.162 (d, J = 7.32 Hz, CH_3, 6H), 0.8–2.1 (m, ring, OH, 18 H); ^{13}C NMR 21.518, 22.318, 22.900, 27.849, 35.418, 39.954, 40.415, 77.992; IR (KBr) 3492 (m), 2950 (s), 2920 (s), 2875 (m), 2841 (m), 1453 (m), 1380 (m), 1287 (w), 1253 (w), 1139 (m), 1019 (w), 998 (m), 948 (w), 937 (w) cm^{-1}. Anal. ($C_{16}H_{30}O_2$) C, H.

3,3,3′,3′,5,5,5′,5′-Octamethyl-[1,1′-bicyclohexyl]-1,1′-diol (11b). A mixture of 22.8 g (0.85 mol) of finely cut aluminum foil, 10.5 g (39 mmol) of $HgCl_2$, and 320 mL of THF was stirred under N_2 for 45 min

(56) Mandelbaum, A.; Cais, M. *J. Org. Chem.* **1961**, *26*, 2633–2640.
(57) Eisenbraun, E. J.; McElvain, S. M. *J. Am. Chem. Soc.* **1955**, *77*, 3383–3384.
(58) Leffler, M. T.; Calkins, A. E. "Organic Syntheses"; Horning, E. C., Ed.; Wiley: New York, 1955; Collect. Vol. III, p 544.
(59) Späth, E. *Sitzungsber. Akad. Wiss. Wien.* **1911**, *120*, 1117.

and the cloudy supernatant was decanted. The amalgam was washed with three 120-mL portions of anhydrous CH_2Cl_2 and then stirred vigorously in 175 mL of CH_2Cl_2 as 190.4 g (1.23 mol) of ketone **10b** was added (20 min). The reaction mixture was stirred under reflux for 5 h, cooled to ambient temperature, and quenched by dropwise addition of 210 mL of saturated aqueous NaCl. The resulting viscous suspension was stirred vigorously for 16 h and filtered. The gray precipitate was exhaustively extracted with hot $CHCl_3$ (750 mL). Evaporation of solvents from the combined filtrates and recrystallization of the resulting residue from CH_2Cl_2/pentane furnished 80 g (42%) of pinacol **11b** as colorless plates: mp 167–168 °C; M^+ *m/e* 310; ^1H NMR (200 MHz, $CDCl_3$) δ 0.92 (s, CH_3, 12 H), 1.12 (AB q, CH_2, 4 H), 1.21 (s, CH_3, 12 H), 1.43 (AB q, CH_2, 8 H), 1.69 (s, OH, 2H); IR (KBr) 3420 (m, br), 2950 (s), 2900 (s), 2870 (m), 1380 (w), 1365 (m), 1211 (m), 1045 (w), 990 (w) cm^{-1}. Anal. ($C_{20}H_{38}O_2$) C, H.

(3*R*,3'*R*,5*R*,5'*R*)-Tetramethylbi-1-cyclohexen-1-yl (12a). A solution of 2.34 g (9.2 mmol) of diol **11a** in 8 mL of pyridine was stirred under N_2 as 1.6 mL (0.96 g, 6.2 mmol) of $POCl_3$ was added in one portion. The reaction mixture was stirred vigorously and heated by means of a steam bath for 7.5 h, cooled to ambient temperature, and quenched by dropwise addition of 8 mL of water. The pH was adjusted to ~4 by addition of 4.5 mL of 6 N aqueous HCl. The mixture was poured into 80 mL of water and extracted with four 30-mL portions of pentane. The combined extracts were washed with 15 mL of each of the following aqueous solutions: 1.2 N HCl, 10% $NaHCO_3$, and water. Drying ($MgSO_4$) and evaporation of the solvent gave 1.96 g (98%) of diene **12a** as a colorless oil, which crystallized upon standing at −16 °C. An analytical sample was prepared by microdistillation in vacuo: mp 12–14 °C; $[\alpha]^{25}_{589}$ +225.1°, $[\alpha]^{25}_{578}$ +234.4°, $[\alpha]^{25}_{546}$ +270.2°, $[\alpha]^{25}_{436}$ +491.9° (*c* 0.825, $CHCl_3$); M^+ *m/e* 218; ^1H NMR (200 MHz, $CDCl_3$) δ 0.876 (d, *J* = 6.59 Hz, CH_3, 6 H), 1.012 (d, *J* = 8.30 Hz, CH_3, 6 H), 1.3–2.5 (m, ring, 12 H), 5.677 (d, *J* = 3.66 Hz, C=CH); IR (neat) 2953 (s), 2915 (s), 2870 (m), 1454 (m), 1376 (w), 819 (w) cm^{-1}; UV 224 (sh) (ϵ 11 000), 232 (16 000), 239 (19 000), 247 (13 000), 261 (sh) (1700) nm. Anal. ($C_{16}H_{26}$) C, H.

3,3,3',3',5,5,5',5'-Octamethylbi-1-cyclohexen-1-yl (12b). A mixture of 15.5 g (50 mmol) of diol **11b**, 42.5 mL of pyridine, and 8.5 mL (5.1 g, 33 mmol) of $POCl_3$ was stirred under N_2 with steam bath heating for 18 h. The reaction flask was placed in a cold water bath and 30 mL of cold water was added dropwise. The resulting suspension was poured into 20 mL of water and the pH adjusted to ~4 by addition of 20 mL of 6 N aqueous HCl. The product was extracted with 120 mL and three 30-mL portions of pentane. The combined extracts were washed with two 15-mL portions of 1.2 N aqueous HCl, 10 mL of 10% aqueous $NaHCO_3$, and 10 mL of water, and dried (Na_2SO_4). Solvent removal in vacuo gave 13.3 g (97%) of diene **12b**, which was pure according to its ^1H NMR spectrum (60 MHz). Recrystallization from ethanol afforded 12.3 g (89%) of white blades: mp 110–111 °C; M^+ *m/e* 274; ^1H NMR (200 MHz, $CDCl_3$) δ 0.962 (s, CH_3, 12 H), 1.020 (s, CH_3, 12 H), 1.325 (s, CH_2, 4 H), 1.915 (s, CH_2, 4 H), 5.354 (s, C=CH, 2 H); IR (KBr) 2970 (m), 2950 (s), 2900 (s), 2840 (m), 1463 (m), 1378 (w), 1360 (m), 1329 (w), 1260 (w), 843 (m) cm^{-1}; UV 232 (ϵ 21 000), 239 (22 000), 247 (sh) (15 000) nm. Anal. ($C_{20}H_{34}$) C, H.

[1*R*[1α(1'*S,2'*R**,3'*R**,5'*R**),2β,3α,5β]]-3,3',5,5'-Tetramethyl-[1,1'-bicyclohexyl]-2,2'-diol (14a) and [1*R*[1α-(1'*R**,2'*S**,3'*R**,5'*R**),2β,3α,5β]]-3,3',5,5'-Tetramethyl-[1,1'-bicyclohexyl]-2,2'-diol (15a).** A solution of 0.98 g (4.5 mmol) of diene **12a** in 10 mL of THF was stirred at −40 to −36 °C under N_2 as 13 mL of 1 M BH_3–THF was added dropwise over 13 min. The reaction mixture was stirred at −40 °C for 0.5 h, warmed to −30 °C, over 1 h, stored at −17 °C under N_2 for 45 h, stirred at −16 to −5 °C for 2 h, and stored at 2 °C for 18.5 h. The reaction flask was cooled with an ice–salt bath, and 10 mL of ethanol, followed by 8 mL of 3 N aqueous NaOH, was added dropwise. The cooling bath was removed and 5.5 mL of 30% aqueous H_2O_2 was added at such a rate that the reaction temperature did not exceed 35 °C. The oxidation mixture was stirred vigorously under N_2 at 49–50 °C for 4 h, cooled to ambient temperature, and saturated with K_2CO_3. The aqueous phase was extracted with three 8-mL portions of ether and the combined organic solutions were washed with saturated aqueous K_2CO_3 and dried (K_2CO_3). Evaporation of the solvents left 1.16 g of a white solid, which was chromatographed on alumina with 1:0 to 0:1 (v/v) CH_2Cl_2/ether, affording 0.55 g (48%) of ψ-*meso*-diol **14a** (mp 155.5–156.5 °C (benzene/hexane)), 0.08 g (7%) of a 1:1 mixture of **14a** and **15a**, as determined by 60 MHz ^1H NMR spectroscopy (vide infra), and 0.21 g (18%) of *sym*-diol **15a** (mp 169.5–170 °C (benzene/hexane)), respectively.

The spectral properties of diol **14a** were as follows: $[\alpha]^{25.2}_{589}$ −38.42°, $[\alpha]^{25.2}_{578}$ −40.05°, $[\alpha]^{25.2}_{546}$ −45.12°, $[\alpha]^{25.2}_{436}$ −74.24° (*c* 2.03, $CHCl_3$); M^+ *m/e* 254; ^1H NMR (200 MHz, $CDCl_3$) δ 1.016 (d, *J* = 7.08 Hz, CH_3, 3 H), 1.034 (d, *J* = 6.84 Hz, CH_3, 6 H), 1.142 (d, *J* = 6.59 Hz, CH_3, 3 H), 0.8–2.15 (m, ring, OH, 16 H), 3.162 (apparent t, $J_{1,2} \sim J_{2,3}$ = 9.77 Hz, OCH, 1 H), 3.818 (dd, $J_{1',2'}$ = 10.99, $J_{2',3'}$ = 4.88 Hz, OCH, 1 H); ^{13}C NMR ($CDCl_3$) 12.032, 18.558, 18.825, 22.439, 26.369, 27.679, 34.229, 34.884, 35.418, 36.510, 38.644, 39.348, 39.639, 40.391, 75.008, 78.987; IR (KBr) 3350 (m, br), 2960 (m), 2920 (s), 1455 (w), 1054 (m), 1022 (w) cm^{-1}. Anal. ($C_{16}H_{30}O_2$) C, H.

The spectral properties of diol **15a** include the following: $[\alpha]^{25.2}_{589}$ +34.38°, $[\alpha]^{25.2}_{578}$ +35.63°, $[\alpha]^{25.2}_{546}$ +41.68°, $[\alpha]^{25.2}_{436}$ +70.00° (*c* 2.08, $CHCl_3$); M^+ *m/e* 254; ^1H NMR (200 MHz, $CDCl_3$) δ 0.996 (d, *J* = 6.10 Hz, CH_3, 6 H), 1.018 (d, *J* = 7.32 Hz, CH_3, 6 H), 0.8–2.2 (m, ring, OH, 16 H), 2.888 (t, *J* = 9.77 Hz, OCH, 2 H); ^{13}C NMR ($CDCl_3$) 18.364, 19.189, 27.485, 30.590, 34.908, 36.364, 39.712, 77.580; IR (KBr) 3355 (m, br), 2960 (m, sh), 2918 (s), 2878 (m), 1455 (w), 1362 (w), 1040 (m), 1013 (w) cm^{-1}. Anal. ($C_{16}H_{30}O_2$) C, H.

Hydroboration of 3,3,3',3',5,5,5',5'-Octamethylbi-1-cyclohexen-1-yl (12b) at 3–24 °C. A solution of 2.6 g (9.5 mmol) of diene **12b** in 20 mL of THF was stirred under N_2 at 3–5 °C as 20 mL of 1 M BH_3–THF was added dropwise over 35 min. The reaction mixture was stirred at 1–3 °C for 16 h and at ambient temperature for 16 h and then quenched by dropwise addition of 15 mL of ethanol, followed by 12 mL of 3 N aqueous NaOH and 8 mL of 30% aqueous H_2O_2. The oxidation mixture was stirred under N_2 at 46–50 °C for 3 h, cooled to ambient temperature, and saturated with K_2CO_3. The aqueous phase was extracted with two 10-mL portions of THF, and the combined organic solutions were extracted with saturated aqueous K_2CO_3 and dried (K_2CO_3). Evaporation of the solvent gave 2.9 g of a semisolid residue, which was recrystallized from hexane to afford 0.414 g (14%) of *meso-trans,trans*-3,3,3',3',5,5,5',5'-octamethyl-[1,1'-bicyclohexyl]-2,2'-diol (**14b**), mp 180–181 °C. For the spectral properties of **14b**, vide infra.

The mother liquor was concentrated in vacuo to yield an oily residue, which was chromatographed on alumina with 100:0 to 90:10 (v/v) CCl_4/CH_3OH, affording 0.75 g (27%) of *trans*-6-(3,3,5,5-tetramethylcyclohexen-1-yl)-2,2,4,4-tetramethylcyclohexanol (**13b**, for properties, vide infra), 0.34 g (12%) of *trans*-3,3,3',3',5,5,5',5'-octamethyl-[1,1'-bicyclohexyl]-1,2'-diol (**17**, mp 99–101 °C, CH_3OH/H_2O), and 1.47 g of a light yellow solid. Chromatography of the last fraction on alumina with CH_2Cl_2, followed by $CHCl_3$, gave a colorless solid, which was recrystallized from hexane to afford 0.382 g (18%) of *trans*-6-(3,3,5,5-tetramethylcyclohexen-1-yl)-2,2,4,4-tetramethylcyclohexane-1-borinic acid (**16**): mp 148–149 °C; M^+ *m/e* 320; ^1H NMR (200 MHz, $CDCl_3$) δ 0.7–1.6 (m, CH_3, CH_2, OH, 33 H), 2.010 (apparent dt, *J* = 12.2, 2.9 Hz, C=CCH, 1 H), 4.176 (s, BOH, 2 H), 5.208 (s, C=CH, 1 H); IR (KBr) 3445 (w, sh), 3355 (m, br), 2944 (s), 2892 (m), 2860 (w), 1357 (m, br), 1334 (w), 1317 (w) cm^{-1}. Anal. ($C_{20}H_{37}BO_2$) C, H.

The spectral properties of **17** were as follows: M^+ *m/e* 310; ^1H NMR (200 MHz, $CDCl_3$) δ 0.892 (s, CH_3, 3 H), 0.911 (s, CH_3, 3 H), 0.954 (s, CH_3, 3 H), 0.973 (s, CH_3, 3 H), 0.993 (s, CH_3, 3 H), 1.022 (s, CH_3, 3 H), 1.053 (s, CH_3, 3 H), 1.105 (s, CH_3, 3 H), 1.0–1.8 (m, CH_2, CH, OH, 13 H), 3.049 (dd, *J* = 10.2, 2.9 Hz, OCH, 1 H); ^1H NMR (60 MHz, Me_2SO-d_6) δ 0.9–1.8 (m, CH_3, CH_2, CH, 35 H), 3.31 (s, OH, 1 H), 3.05 (m, OCH, 1 H), 4.02 (d, *J* = 7 Hz, OH, 1 H); IR (KBr) 3400 (m, br), 2950 (s), 2914 (s), 2905 (s), 1475 (w), 1454 (w), 1387 (w), 1367 (m) cm^{-1}. Anal. ($C_{20}H_{38}O_2$) C, H.

***meso-trans,trans*-3,3,3',3',5,5,5',5'-Octamethyl-[1,1'-bicyclohexyl]-2,2'-diol (14b).** A suspension of 47.11 g (0.172 mol) of diene **12b** in 360 mL of THF was stirred vigorously under N_2 at −10 to −5 °C as 380 mL of 1 M BH_3–THF was added dropwise over 1.5 h. The clear reaction mixture was stirred for 1 h at −5 °C and for 45 min at 0 °C and then stored under N_2 at 4 °C for 3 days, producing a copious white precipitate, which dissolved after stirring at 25–30 °C for 3 days. Ethanol (280 mL), 225 mL of 3 N aqueous NaOH, and 155 mL of 30% aqueous H_2O_2 were added, maintaining the internal temperature below 50 °C. The oxidation mixture was stirred under N_2 at 50 °C for 32 h, cooled to ambient temperature, and saturated with K_2CO_3. The aqueous phase was extracted with two 200-mL portions of THF, and the combined THF solutions were extracted with saturated aqueous K_2CO_3 and dried (K_2CO_3). Solvent removal in vacuo, followed by recrystallization (benzene/hexane), produced 41.85 g (78%) of diol **14b** as analytically pure white crystals: mp 181–181.5 °C; M^+ *m/e* 310; ^1H NMR (200 MHz, $CDCl_3$) δ 0.889 (s, CH_3, 6 H), 0.945 (s, CH_3, 6 H), 0.986 (s, CH_3, 6 H), 1.023 (s, CH_3, 6 H), 0.8–1.4 (m, CH_2, OH, 10 H), 1.926 (m, CH, 2 H), 3.390 (d, *J* = 10.5 Hz, OCH, 2 H); IR (KBr) 3400 (m, br), 2960 (s), 2940 (s), 1460 (w), 1364 (w), 1037 (m) cm^{-1}. Anal. ($C_{20}H_{38}O_2$) C, H.

***trans*-6-(3,3,5,5-Tetramethylcyclohexen-1-yl)-2,2,4,4-tetramethylcyclohexanol (13b).** A suspension of 2.6 g (9.5 mmol) of diene **12b** in 30 mL of THF was stirred at −5 to −3 °C under N_2 as 12 mL of 1 M BH_3–THF was added dropwise over 10 min. The clear reaction mixture was stirred at 0–4 °C for 6 h, resulting in the formation of a white precipitate, stored at 0 °C under N_2 for 2 days, and then stirred at 5–7 °C for 1 day. The opaque reaction mixture was quenched at 5 °C by

dropwise addition of 9 mL of ethanol, and 8 mL of 3 N aqueous NaOH and 5 mL of 30% aqueous H_2O_2 were added. The oxidation mixture was stirred under N_2 at 48–49 °C for 22 h, cooled to ambient temperature, and saturated with K_2CO_3. The aqueous layer was extracted with two 15-mL portions of THF, and the combined THF solutions were extracted with saturated aqueous K_2CO_3 and dried (K_2CO_3). Solvent removal in vacuo produced 2.8 g of a colorless viscous oil, which was dissolved in pentane and adsorbed onto 100 g of alumina. Washing with 150 mL of pentane, followed by 300 mL of CCl_4, and evaporation of the CCl_4 filtrate furnished 1.33 g (48%) of alcohol **13b** as an analytically pure white solid: mp 56.5–58.5 °C; M^+ *m/e* 292; ^1H NMR (200 MHz, $CDCl_3$) δ 0.88–1.70 (m, CH_3, CH_2, OH, 33 H), 2.220 (m, C=CCH, 1 H), 3.138 (dd, J = 10.8, 2.0 Hz, OCH), 5.342 (s, C=CH, 1 H); IR (KBr) 3565 (m), 3475 (w, sh), 2950 (s), 2910 (s), 2864 (m), 1453 (m), 1385 (m), 1362 (m), 1053 (m), 986 (m), 970 (w), 624 (w) cm^{-1}. Anal. ($C_{20}H_{36}O$) C, H.

***trans*-1-(Benzyloxy)-6-(3,3,5,5-tetramethylcyclohexen-1-yl)-2,2,4,4-tetramethylcyclohexane (18).** A mixture of 0.144 g (6 mmol) of sodium hydride, 0.876 g (3 mmol) of alcohol **13b**, and 4 mL of DMF was stirred under N_2 for 20.5 h. Freshly distilled benzyl bromide (0.48 mL, 0.68 g, 4 mmol) was added dropwise, causing the mixture to froth and warm. The light brown reaction mixture was stirred at ambient temperature for 1 day, quenched by addition of several drops of water, and distributed between 15 mL of water and 20 mL of ether. The organic phase was washed with three 5-mL portions of water, dried (Na_2SO_4), and concentrated in vacuo to afford 1.16 g of viscous yellow oil. Chromatography on silica with CCl_4 furnished 0.767 g (67%) of benzyl ether **18** as a light yellow oil: M^+ *m/e* 382; ^1H NMR (200 MHz, $CDCl_3$) δ 0.884 (s, CH_3, 3 H), 0.911 (s, CH_3, 3 H), 0.941 (s, CH_3, 3 H), 0.972 (s, CH_3, 3 H), 0.995 (s, CH_3, 3 H), 1.010 (s, CH_3, 3 H), 1.045 (s, CH_3, 3 H), 1.075 (s, CH_3, 3 H), 0.9–1.94 (m, CH_2, 8 H), 2.330 (m, C=CCH, 1 H), 3.037 (d, J = 10.74 Hz, OCH, 1 H), 4.603 (AB q, $PhCH_2$, 2 H), 5.311 (s, C=CH, 1 H), 7.289 (m, Ar H, 5 H); ^{13}C NMR (CD_2Cl_2/CS_2)[60] 22.536, 27.121, 30.178, 30.348, 30.445, 30.736, 31.488, 31.779, 32.288, 32.555, 35.005, 37.407, 42.089, 44.733, 45.679, 50.289, 53.345, 75.227, 89.515, 126.728, 126.777, 127.868, 131.264, 135.825, 139.706; IR (neat) 2950 (s), 2897 (s), 2865 (s), 1478 (w), 1453 (m), 1383 (w), 1364 (m), 1100 (m), 1074 (m), 732 (m), 697 (m) cm^{-1}. Anal. ($C_{27}H_{42}O$) C, H.

Hydroboration/Oxidation/Hydrogenolysis of Benzyl Ether 18. A solution of 0.38 g (1 mmol) of benzyl ether **18** in 2 mL of THF was stirred at −16 °C under N_2 as 1.2 mL of 1 M BH_3–THF was added dropwise. The reaction mixture was warmed gradually to ambient temperature (16 h) and stirred for 7.6 days. Oxidation and product isolation were carried out as in the preparation of **14b**, producing 0.35 g of viscous, light yellow oil, shown by ^1H NMR (60 MHz) and analytical TLC (silica/CCl_4) to contain only a trace of unreacted **18**.

A 100-mg portion of the crude product obtained above was dissolved in 5 mL of CH_3OH containing 10 drops of 70% aqueous $HClO_4$ and hydrogenolyzed over $PdCl_2$ at atmospheric pressure. The catalyst was removed by filtration, and the filtrate was concentrated at reduced pressure, diluted with ether, and extracted with water and saturated aqueous NaCl. After drying (Na_2SO_4), evaporation of the solvents afforded 61 mg (68%, from **18**) of a white solid, identical with *meso*-diol **14b**, according to its 60-MHz ^1H NMR spectrum. Recrystallization from hexane furnished a crystalline sample, mp 178–180 °C; mmp with **14b**, 178.5–180.5 °C.

Asymmetric Hydroboration of Bi-1-cyclohexen-1-yl (4). A solution of monoisopinocampheylborane in THF (prepared from 20 mmol of (+)-α-pinene[29]) was stirred at −20 to −16 °C under N_2 as a solution of 1.46 g (9 mmol) of diene **4** in 5 mL of THF was added dropwise over 5 min. The reaction mixture was warmed to 0 °C over 1 h and then stirred at 0 °C for 4 h and at ambient temperature for 16 h. Methanol (3.6 mL), 7.3 mL of 30% aqueous NaOH, and 5.5 mL of 30% aqueous H_2O_2 were added, and the resulting mixture was heated under reflux for 16 h and then cooled to ambient temperature. The aqueous phase was saturated with K_2CO_3 and extracted with two 5-mL portions of ether. The combined organic solutions were dried (K_2CO_3) and concentrated in vacuo, producing 4.44 g of semisolid residue. Chromatography on alumina with 99:1 to 95:5 (v/v) ether/CH_3OH gave 0.75 g (42%) of a white solid: mp 151–153 °C, with spectral properties identical with those of **5**; $[\alpha]^{25}_{589}$ +0.8°, $[\alpha]^{25}_{578}$ +1.2°, $[\alpha]^{25}_{546}$ +1.1°, $[\alpha]^{25}_{436}$ +1.9° (*c* 1.60, $CHCl_3$).

(60) The ^{13}C NMR spectrum of **18** was found to be temperature dependent in the range from −60 to −90 °C. Coalescence phenomena were observed mainly for the olefinic and ether carbon signals. The intensities of these resonances at −99 °C implied the presence of only ~11% of the minor conformer, which is probably related to the major one by rotation about the interannular bond. For a similar case, see: Leete, E.; Riddle, R. M. *Tetrahedron Lett.* 1978, 5163–5166.

(−)-Menthoxyacetaldehyde (19). Allyl menthyl ether (35.7 g, 0.182 mol) was dissolved in 136 mL of anhydrous methanol and ozonized at −78 °C, decomposing the ozonide with 18.5 mL (0.25 mol) of dimethyl sulfide.[31] Solvent and excess dimethyl sulfide were removed under reduced pressure, and the liquid residue was dissolved in 500 mL of ether. This solution was extracted with two 50-mL portions of water and then saturated aqueous NaCl and dried (Na_2SO_4). Evaporation of the solvent left a colorless oil, which was dissolved in CH_2Cl_2 and filtered through Florisil, washing thoroughly with additional CH_2Cl_2. Concentration of the combined filtrates in vacuo furnished 34.69 g (96%) of aldehyde **19** as a light yellow oil which was suitably pure for the preparation of acetals. Fractional distillation gave an analytical sample: bp 54 °C (0.1 mm); $[\alpha]^{25}_{589}$ −98.33°, $[\alpha]^{25}_{578}$ −101.91°, $[\alpha]^{25}_{546}$ −115.14°, $[\alpha]^{25}_{436}$ −192.19° (*c* 1.26, $CHCl_3$); M^+ *m/e* 169; ^1H NMR (200 MHz, $CDCl_3$) δ 0.7–2.3 (m, CH_3, CH_2, CH, 18 H), 3.145 (apparent dt, J = 4.4, 10.3 Hz, OCH, 1 H), 4.066 (m, OCH_2, 2 H), 9.756 (d, J = 1.1 Hz, CHO, 1 H); IR (neat) 2960 (s), 2930 (s), 2870 (m), 1736 (m), 1454 (m), 1370 (w), 1180 (w), 1119 (m), 1009 (w) cm^{-1}. Anal. ($C_{12}H_{22}O_2$) C, H.

Resolution of *d,l*-*trans,trans*-[1,1′-Bicyclohexyl]-2,2′-diol (5). According to the method of Roelofsen and van Bekkum,[33] a mixture of 2.25 g (11.4 mmol) of *d,l*-diol **5**, 2.70 g (13.6 mmol) of aldehyde **19**, 8 g of Linde 5-Å molecular sieve powder, 0.20 g of *p*-toluenesulfonic acid monohydrate, and 55 mL of CH_2Cl_2 was stirred under N_2 for 17 h. The reaction mixture was filtered through alumina, rinsing well with CH_2Cl_2, and the combined filtrates were concentrated in vacuo to afford 4.26 g of a viscous yellow oil. Four recrystallizations from pentane produced 83 mg of acetal **20** as fine white needles: mp 95.5–96.5 °C; $[\alpha]^{25}_{589}$ −53.7°, $[\alpha]^{25}_{578}$ −55.7°, $[\alpha]^{25}_{546}$ −63.1°, $[\alpha]^{25}_{436}$ −104.4° (*c* 1.69, $CHCl_3$); M^+ *m/e* 378; ^1H NMR (200 MHz, C_6D_6) 0.6–2.6 (m, CH_3, CH_2, CH, 36 H), 3.10 (m, OCH, 1 H), 3.32 (m, OCH, 2 H), 3.75 (m, OCH_2, 2 H), 4.795 (t, J = 4.64 H_2, O_2CH, 1 H); IR (KBr) 2970 (s), 2865 (s), 1452 (m), 1367 (m), 1135 (s), 1096 (m), 1057 (m), 1004 (w), 976 (w), 919 (w), 910 (w), 892 (w), 661 (w) cm^{-1}. Anal. ($C_{24}H_{42}O_3$) C, H.

A solution of 75 mg of acetal **20** in 10 mL of THF and 14 mL of 1.2 N aqueous HCl was stirred under N_2 for 8 h, neutralized with $NaHCO_3$, and saturated with NaCl. The aqueous phase was extracted with CH_2Cl_2 and the combined organic solutions were dried (Na_2SO_4). The solvents were evaporated, leaving 77 mg of semicrystalline residue. Chromatography on alumina with 99:1 to 97:3 (v/v) ether/CH_3OH afforded 28.3 mg (72%) of a white crystalline solid: mp 153.5–155 °C, with spectral properties identical with those of other samples of diol **5**; $[\alpha]^{25}_{589}$ −3.1°, $[\alpha]^{25}_{578}$ −3.3°, $[\alpha]^{25}_{546}$ −4.4°, $[\alpha]^{25}_{436}$ −6.5° (*c* 1.42, $CHCl_3$).

1,2,3,4,4a,7a,8,9,10,11,11a,11b-Dodecahydro-6-phenyl-2,2,4,4,8,8,10,10-octamethyldibenzo[*d,f*][1,3]dioxepin (21). A mixture of 0.31 g (1 mmol) of diol **14b**, 5 mL of CH_2Cl_2, 0.13 mL (0.14 g, 0.13 mmol) of freshly distilled benzaldehyde, 1.3 g of Linde 5-Å molecular sieve powder, and 50 mg of *p*-toluenesulfonic acid monohydrate was stirred under N_2 for 3 days. The reaction mixture was diluted with 15 mL of pentane and filtered through alumina, rinsing well with pentane. The combined filtrates were concentrated in vacuo to afford 0.35 g of semisolid residue: ^1H NMR (60 MHz, $CDCl_3$) δ 0.8–3.6 (m, CH_2, CH), 3.47 (d, J = 9 Hz, OCH), 3.73 (d, J = 11 Hz, OCH), 5.47 (s, O_2CHPh), 6.33 (s, O_2CHPh), 7.2–8.0 (m, Ar H), 10.34 (s, CHO). Analytical TLC (silica, 1:3 (v/v) benzene/cyclohexane) showed that this crude product consisted of three components: R_f 0.16 (benzaldehyde), 0.30, and 0.36. Preparative TLC of a 115-mg sample under the same conditions furnished 20 mg (15%) of the highest R_f component. Recrystallization from CH_3OH/H_2O gave 10 mg of acetal **21** as minute, white crystals: mp 99–102.5 °C; M^+ *m/e* 398; ^1H NMR (200 MHz, $CDCl_3$) δ 0.892 (s, CH_3, 6 H), 0.912 (s, CH_3, 6 H), 1.057 (s, CH_3, 6 H), 1.078 (s, CH_3, 6 H), 0.7–1.5 (m, CH_2, 8 H), 2.351 (m, CH, 2 H), 3.730 (d, J = 11.23 Hz, OCH, 2 H), 6.324 (s, O_2CHPh, 1 H), 7.31 (m, *m,p*-Ar H, 3 H), 7.51 (m, *o*-Ar H, 2 H); IR (KBr) 2952 (s), 2900 (m), 2854 (m), 1457 (w), 1372 (w), 1367 (w), 1103 (s), 1076 (w), 1027 (m), 1011 (w), 760 (w), 701 (m) cm^{-1}. Anal. ($C_{27}H_{42}O_2$) C, H.

1,2,3,4,4a,7a,8,9,10,11,11a,11b-Dodecahydro-2,2,4,4,8,8,10,10-octamethyldibenzo[*d,f*][1,3]dioxepin (22). According to the method of Hanessian et al.,[36] a solution of 0.31 g (1 mmol) of diol **14b** and 0.53 g (3 mmol) of *N*-bromosuccinimide in 10 mL of Me_2SO was stirred under N_2 at 49–59 °C for 26 h. The cooled reaction mixture was diluted with 10 mL of 10% aqueous $NaHCO_3$, followed by 10 mL of water, and extracted with one 15-mL and two 10-mL portions of ether. The combined extracts were washed with three 5-mL portions of water, dried (Na_2SO_4), and concentrated in vacuo to yield 0.31 g (96%) of acetal **22** as a white solid which was pure according to its ^1H NMR spectrum (200 MHz). Sublimation at 46 °C (0.1 mm), followed by recrystallization from CH_3OH, gave 0.175 g (54%) of white blades: mp 80–81 °C; M^+ *m/e* 322; ^1H NMR (200 MHz, $CDCl_3$) δ 0.915 (s, CH_3, 6 H), 0.955 (s, CH_3, 6 H), 1.003 (s, CH_3, 6 H), 1.010 (s, CH_3, 6 H), 0.9–1.4 (m, CH_2, 8 H), 2.198 (m, CH, 2 H), 3.392 (d, J = 10.25 Hz, OCH, 2 H), 5.007

(AB q, $\Delta\nu$ = 0.57 ppm, J = 5.6 Hz); IR (KBr) 2949 (m), 2915 (m), 2860 (m), 1460 (w), 1362 (w), 1181 (m), 1127 (m), 1083 (s), 971 (w) cm^{-1}. Anal. ($C_{21}H_{38}O_2$) C, H.

1,2,3,4,4a,5a,6,7,8,9,9a,9b-Dodecahydro-2,2,4,4,6,6,8,8-octamethyldibenzofuran (23). A mixture of 0.31 g (1 mmol) of diol **14b**, 2 mL of 2,2-dimethoxypropane, 15 mg of *p*-toluenesulfonic acid monohydrate, and 6 mL of benzene was heated with stirring for 1 day, while the refluxing solvent was passed through Linde 5-Å molecular sieve pellets contained in a Sohxlet extractor. The reaction mixture was filtered through alumina, washing thoroughly with CH_2Cl_2. The solvents were removed from the combined filtrates by evaporation, affording 0.282 g of residue. Sublimation at 60–80 °C (0.1 mm) gave a light yellow solid, which was recrystallized from CH_3OH, furnishing 75 mg (25%) of **23** as minute white needles: mp 70.5–71.5 °C; M^+ m/e 292; ^1H NMR (200 MHz, $CDCl_3$) δ 0.895 (s, CH_3, 3 H), 0.927 (s, CH_3, 3 H), 0.952 (s, CH_3, 9 H), 0.965 (s, CH_3, 3 H), 0.992 (s, CH_3, 3 H), 1.027 (s, CH_3, 3 H), 0.9–1.5 (m, CH_2, CH, 9 H), 2.18 (m, CH, 1 H), 3.230 (d, J = 10.74 Hz, OCH, 1 H), 3.51 (m, OCH, 1 H); IR (KBr) 2960 (s), 2902 (s), 2860 (m), 1463 (m), 1371 (m), 1365 (m), 1158 (w), 1118 (w), 1060 (s), 1000 (w), 980 (w), 964 (m) cm^{-1}. Anal. ($C_{20}H_{36}O$) C, H.

***trans*-*transoid*-*trans*-2,5,8,11,14,17-Hexaoxatricyclo[22.4.0.0^{18,23}]octacosane (24a).** A suspension of 0.29 g (12 mmol) of NaH in 60 mL of THF was stirred under N_2 at reflux temperature as a solution of 0.72 g (3.6 mmol) of diol **5** and 2.0 g (3.7 mmol) of pentaethylene glycol ditosylate in 180 mL of THF was added dropwise over 20 h. The reaction mixture was stirred under reflux for 20 h, cooled to ambient temperature, and quenched by the addition of several drops of water. The resulting suspension was filtered through Celite, rinsing with 100 mL of THF, and the combined filtrates were concentrated in vacuo. A solution of the residue in 100 mL of CH_2Cl_2 was washed with 25 mL of 0.24 N aqueous HCl, followed by saturated aqueous NaCl, and dried ($MgSO_4$). Solvent removal at reduced pressure afforded 1.44 g of a viscous, light yellow oil, which was purified by gel permeation and alumina chromatography with ether. Thus obtained was 0.56 g (39%) of host **24a** as a viscous oil: M^+ m/e 400; ^1H NMR (200 MHz, $CDCl_3$) δ 0.9–2.2 (m, CH_2, CH, 18 H), 3.3–3.9 (m, OCH_2, OCH, 22 H); IR (neat) 2930 (s), 2860 (s), 1728 (w), 1450 (m), 1354 (m), 1297 (w), 1250 (w), 1110 (s, br), 949 (w) cm^{-1}. Anal. ($C_{22}H_{40}O_6$) C, H.

***trans*-*cisoid*-*trans*-2,5,8,11,14,17-Hexaoxatricyclo[22.4.0.0^{18,23}]octacosane (25a).** A suspension of 0.31 g (13 mmol) of NaH in 70 mL of THF was stirred under N_2 at reflux temperature as a solution of 0.83 g (4.2 mmol) of diol **6** and 2.2 g (4.0 mmol) of pentaethylene glycol ditosylate in 210 mL of THF was added dropwise over 19 h. The reaction mixture was stirred under reflux for 21 h, cooled to ambient temperature, quenched by the addition of several drops of water, and worked up as in the preparation of **24a** above. The resulting yellow oil (1.31 g) was purified by gel permeation and alumina chromatography (99:1 to 96:4 (v/v) ether/methanol), yielding 124 mg (7.4%) of host **25a**, free of higher and lower R_f contaminants: M^+ m/e 400; ^1H NMR (200 MHz, $CDCl_3$) δ 0.9–2.2 (m, CH_2, CH, 18 H), 3.12 (m, OCH, 2 H), 3.3–3.8 (m, OCH_2, 20 H); IR (neat) 2927 (s), 2836 (m), 1442 (w), 1351 (w), 1110 (m), 1030 (w) cm^{-1}. Anal. ($C_{22}H_{40}O_6$) C, H.

(1*S*,18*S*,19*R*,21*R*,23*R*,24*R*,26*R*,28*R*)-19,21,26,28-Tetramethyl-2,5,8,11,14,17-hexaoxatricyclo[22.4.0.0^{18,23}]octacosane (24b). A suspension of 0.09 g (3.8 mmol) of NaH in 15 mL of THF was stirred under N_2 at reflux temperature as a solution of 0.206 g (0.81 mmol) of diol **15a** and 0.47 g (0.86 mmol) of pentaethylene glycol ditosylate in 43 mL of THF was added dropwise over 30 h. The reaction mixture was stirred under reflux for 67 h and then worked up as usual, affording 0.35 g of a light yellow oil. Gel permeation and alumina chromatography ($CHCl_3$) furnished 0.21 g (56%) of host **24b** as a light yellow oil: $[\alpha]^{25.2}_{589}$ +7.50°, $[\alpha]^{25.2}_{578}$ +7.76°, $[\alpha]^{25.2}_{546}$ +9.01°, $[\alpha]^{25.2}_{436}$ +15.50° (*c* 5.05, $CHCl_3$); M^+ m/e (16 eV) 456; ^1H NMR (200 MHz, $CDCl_3$) δ 0.976 (d, J = 6.10 Hz, equatorial CH_3, 6 H), 1.008 (d, J = 7.08 Hz, axial CH_3, 6 H), 0.8–2.05 (m, CH_2, CH, 12 H), 2.31 (m, 1,1'-CH, 2 H), 2.689 (apparent t, $J_{1,2} \sim J_{2,3}$ = 10.4 Hz, OCH, 2 H), 3.688 (m, OCH_2, 20 H); IR (neat) 2920 (s), 2875 (s), 1460 (m), 1381 (w), 1354 (w), 1112 (s), 1040 (w), 1019 (w), 859 (w) cm^{-1}. Anal. ($C_{26}H_{48}O_6$) C, H.

(1*S*,18*R*,19*R*,21*R*,23*R*,24*S*,26*R*,28*R*)-19,21,26,28-Tetramethyl-2,5,8,11,14,17-hexaoxatricyclo[22.4.0.0^{18,23}]octacosane (25b). A suspension of 0.084 g (3.5 mmol) of NaH in 15 mL of THF was stirred under N_2 at reflux temperature as a solution of 0.19 g (0.75 mmol) of diol **14a** and 0.44 g (0.80 mmol) of pentaethylene glycol ditosylate in 40 mL of THF was added dropwise over 25 h. The reaction mixture was stirred under reflux for 86 h and then worked up as usual, affording 0.33 g of a light yellow oil. Gel permeation and alumina chromatography ($CHCl_3$) furnished 0.19 g (55%) of host **25b** as a yellowish oil: $[\alpha]^{25.2}_{589}$ −24.64°, $[\alpha]^{25.2}_{578}$ −25.66°, $[\alpha]^{25.2}_{546}$ −28.98°, $[\alpha]^{25.2}_{436}$ −47.79° (*c* 4.70, $CHCl_3$); M^+ m/e (16 eV) 456; ^1H NMR (200 MHz, $CDCl_3$) δ 0.820 (d, J = 6.35 Hz, CH_3, 3 H), 0.948 (d, J = 5.4 Hz, CH_3, 3 H), 0.976 (d, J = 6.1 Hz, CH_3, 6 H), 0.8–2.3 (m, CH_2, CH, 14 H), 3.07–3.25 (m, OCH, 2 H), 3.66 (m, OCH_2, 20 H); IR (neat) 2920 (s), 2873 (s), 1460 (m), 1380 (w), 1350 (w), 1102 (s), 1044 (w) cm^{-1}. Anal. ($C_{26}H_{48}O_6$) C, H.

***trans*-*cisoid*-*trans*-19,19,21,21,26,26,28,28-Octamethyl-2,5,8,11,14,17-hexaoxatricyclo[22.4.0.0^{18,23}]octacosane (25c).** A suspension of 0.24 g (12 mmol) of NaH in 60 mL of THF was stirred under N_2 at reflux temperature as a solution of 2.0 g (3.66 mmol) of pentaethylene glycol ditosylate and 1.12 g (3.6 mmol) of diol **14b** in 180 mL of THF was added dropwise over 12 h. The reaction mixture was stirred for 14 h under reflux and then worked up as usual, affording 1.89 g of a semicrystalline residue. Gel permeation chromatography gave 1.16 g of a viscous yellow oil as the major component. Medium-pressure chromatography on silica with ether furnished 0.256 g (14%) of host **25c** (mp 91–92 °C (CH_3OH/H_2O), R_f 0.47) and 0.57 g (31%) of diol **26** as an oil (R_f 0.20).

The spectral properties of host **25c** include the following: M^+ m/e 512; ^1H NMR (200 MHz, $CDCl_3$) δ 0.7–1.6 (m, CH_3, CH_2, CH, 33 H), 2.39 (m, CH, 1 H), 2.826 (d, J = 10.99 Hz, OCH, 1 H), 3.380 (d, J = 10.99 Hz, OCH, 1 H), 3.657 (m, OCH_2, 20 H); IR (KBr) 2943 (s), 2882 (s), 1450 (w), 1380 (w), 1360 (w), 1295 (w), 1130 (m), 1103 (s) cm^{-1}. Anal. ($C_{30}H_{56}O_6$) C, H.

Recrystallization of **26** from CH_3OH/H_2O produced small prisms of a hydrate: IR (KBr) 3540 (m), 3455 (m), 3230 (m, br), 2948 (s), 2879 (s), 1645 (vw), 1499 (m), 1382 (w), 1321 (m), 1284 (m), 1139 (m), 1110 (s), 1083 (s), 1061 (m), 1031 (w), 985 (w), 939 (w) cm^{-1}. These crystals turned to a viscous oil at 42 °C in vacuo: ^1H NMR (200 MHz, $CDCl_3$) δ 0.7–2.2 (m, CH_3, CH_2, CH, OH, 36 H), 3.18 (m, OCH, 2 H), 3.66 (m, OCH_2, 20 H). Anal. ($C_{30}H_{58}O_7$) C, H.

Acknowledgment. Professor D. J. Cram, who suggested the topic of this research, is warmly thanked for helpful discussions, encouragement, and the provision of laboratory facilities.