s, 1 H, O*H*), 3.68 (m, 1 H, 4-C^{2}H$_S$*H*$_R$-OH), 4.35 (m, 1 H, C*α*-H), 5.13 (d, 1 H, N*H*).

9a. (4*R*)-[4-^{2}H], viscous oil; 80.7% yield from **7a** via reduction with (*S*)-Alpine borane: ^{1}H NMR ($CDCl_3$) *δ* 1.46 (s, 18 H, -NCOO-*t*-C$_4$*H*$_9$, O-*t*-C$_4$*H*$_9$), 2.13 (m, 2 H, 3-C*H*$_2$), 3.47 (br s, 1H, O*H*), 3.64 (m, 1 H, 4-C^{2}H$_R$*H*$_S$-OH), 4.32 (m, 1 H, C*α*-*H*), 5.13 (d, 1H, N*H*).

9b. (2*S*,3*R*,4*R*)-[3,4-^{2}H$_2$], oil; 82.1% yield from **7b** via reduction with (*S*)-Alpine borane: ^{1}H NMR ($CDCl_3$) *δ* 1.45 (s, 18 H, -NCOO-*t*-C$_4$*H*$_9$, O-*t*-C$_4$*H*$_9$), 2.13 (m, 1 H, 3-C^{2}H$_R$*H*$_S$), 3.39 (br s, 1 H, O*H*), 3.65 (br s, 1 H, 4-C^{2}H$_R$*H*$_S$-OH), 4.36 (br s, 1 H, C*α*-*H*), 5.36 (d, 1 H, N*H*).

8c. (2*S*,3*S*,4*S*)-[2,3,4-^{2}H$_3$], viscous oil; 85% yield from **7c** via reduction with (*R*)-Alpine borane: ^{1}H NMR ($CDCl_3$) *δ* 1.46 (s, 18 H, -NCOO-*t*-C$_4$*H*$_9$, O-*t*-C$_4$*H*$_9$), 2.10 (br s, H, 3-C^{2}H$_S$*H*$_R$), 3.41 (br s, 1 H, O*H*), 3.68 (br s, 1 H, 4-C^{2}H$_S$*H*$_R$), 5.33 (d, 1 H, N*H*).

(4*S*)-[4-^{2}H]-L-Homoserine Lactone Hydrochloride (10a). A solution of *N*-(*tert*-butyloxycarbonyl)-(4*S*)-[4-^{2}H]-L-homoserine 1-*tert*-butyl ester (**8a**) (0.2 g, 0.72 mmol) in 95% ethanolic HCl (25 mL) was heated to reflux for 3 h. The solvent was removed and the residue was dissolved in absolute ethanol (20 mL) and evaporated under vacuum at 40 °C. This procedure was repeated twice more and the residue dried in vacuum. The off-white solid recrystallized from absolute ethanol to yield 52 mg (52%) of **10a**: mp 203–205 °C; ^{1}H NMR (Me_2SO-d_6) *δ* 2.30 and 2.55 (m, 2 H, 3-C*H*$_2$-), 4.42 (d, 1 H, *J* = 8.9 Hz, 4-C^{2}H$_S$*H*$_R$), 4.32 (dd, 1 H, *J* = 11.02 Hz, 8.9 Hz, C*α*-*H*).

11a. (4*R*)-[4-^{2}H]; 57% yield from **9a**; mp 203–205 °C (ethanol): ^{1}H NMR (Me_2SO-d_6) *δ* 2.30 and 2.55 (m, 2 H, 3-C*H*$_2$), 4.27 (m, 1 H, 4-C^{2}H$_R$*H*$_S$), 4.32 (dd, 1 H, *J* = 11.02 Hz, 8.9 Hz, C*α*-*H*).

13b. (2*S*,3*R*)-[3-^{2}H]; 52% yield from **12b**; mp 203–205 °C (ethanol): ^{1}H NMR (Me_2SO-d_6) *δ* 2.53 (m, 1 H, 3-C^{2}H$_R$*H*$_S$), 4.24 and 4.43 (m, d, 3 H, 4-C*H*$_2$ and C*α*-*H*).

13c. (2*S*,3*S*)-[2,3-^{2}H$_2$]; 55.8% yield **12c**; mp 203–205 °C (ethanol): ^{1}H NMR (Me_2SO-d_6) *δ* 2.30 (t, 1 H, *J* = 9.53 Hz, 3-C^{2}H$_S$*H*$_R$), 4.26 and 4.44 (dd, t, 2 H, *J* = 8.9 Hz, 4-C*H*$_2$).

11b. (2*S*,3*R*,4*R*)-[3,4-^{2}H$_2$]; 52% yield from **9b**; mp 203–205 °C (ethanol): ^{1}H NMR (D_2O) *δ* 2.59 (m, 1 H, 3-C^{2}H$_R$*H*$_S$), 4.27 (br s, 1 H, 4-C^{2}H$_R$*H*$_S$), 4.32 (br s, 1 H, C*α*-*H*).

10c. (2*S*,3*S*,4*S*)-[2,3,4-^{2}H$_3$]; 49% yield from **8c**; mp 203–205 °C (ethanol): ^{1}H NMR (D_2O) *δ* 2.28 (d, 1 H, *J* = 7.3 Hz, 3-C^{2}H$_S$*H*$_R$), 4.46 (d, 1 H, *J* = 9.2 Hz, 4-C^{2}H$_S$*H*$_R$).

(4*S*)-[4-^{2}H]-L-Homoserine. The lactone hydrochloride **10a** (20 mg) was dissolved in water (0.2 mL) and applied to a column of Dowex 50W × 4-200 (NH_4^+, 10 mL) and eluted with water followed by 1 N NH_4OH. Ninhydrin-positive fractions were combined and freeze-dried to yield 15 mg (92%) of (4*S*)-[4-^{2}H]-L-homoserine: ^{1}H NMR (D_2O) *δ* 1.81 and 1.91 (m, 2 H, 3-C*H*$_2$), 3.56 (m, 1 H, 4-C^{2}H$_S$*H*$_R$), 3.67 (m, 1 H, C*α*-*H*).

(4*R*)-[4-^{2}H]-L-Homoserine. The title homoserine was prepared from (4*R*)-[4-^{2}H]-L-homoserine lactone hydrochloride (**11a**) as described above in 93% yield: ^{1}H NMR (D_2O) *δ* 1.83 and 1.96 (m, 2 H, 3-C*H*$_2$), 3.57 (m, 1 H, 4-C^{2}H$_R$*H*$_S$), 3.67 (m, 1 H C*α*-H).

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Hydroboration of Vinyl Ethers with Diisopinocampheylborane[1]

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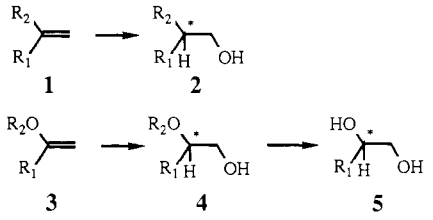
The reactions of diisopinocampheylborane with cyclic vinyl ethers having an exocyclic oxygen and with acyclic vinyl ethers having groups of varying size attached to oxygen were explored. Evidence of some interaction of the bulkier vinyl ethers with diisopinocampheylborane was obtained, but high enantiomeric excesses were not found. However, the hydroboration–oxidation of benzyl or diphenylmethyl vinyl ethers, followed by cleavage, is a practical route to partially resolved diols.

In the course of synthetic studies directed towards the partial synthesis of vitamin D and analogues of the vitamin, we envisioned the need for resolved terminal epoxides derivable from resolved 1,2-diols. Some examples of such diols have been obtained from resolved precursors, including sugars,[2] malic acid,[3] and amino acids.[4] Others have been made in a recent study of osmium tetraoxide hydroxylation in the presence of resolved amine catalysts.[5] As a possible alternative to these methods, we became intrigued with the possibilities for the formation of resolved diols by hydroboration–oxidation. The only major variable for effecting chiral discrimination in the hydroboration–

Scheme I



oxidation of a specific alkene, e.g., **1** to **2** (Scheme I), is the chiral hydroborating reagent. However, a second variable, the structure of a potentially *cleavable* R_2 group, is present in the vinyl ether **3**, which may be converted via **4** to the specified diol **5**.

R^2 in **3** may interact with a resolved chiral hydroborating agent as a consequence of its bulk, as reported here, or may be a resolved (and bulky) chiral group which can interact with a racemic reagent. The most promising approach, not yet tested in our work, is to combine the types of interaction to provide new examples of double asymmetric induction, a subclass of "double stereodifferentiation".[6]

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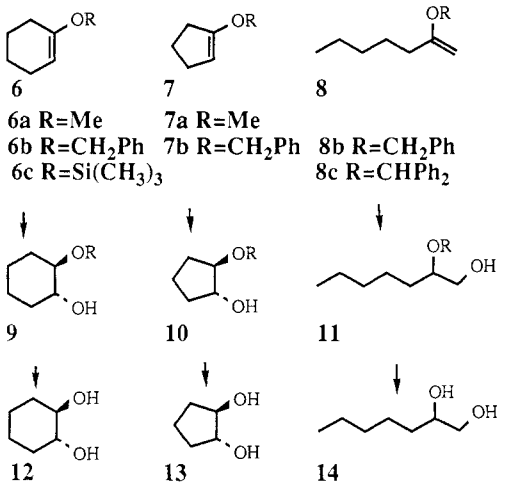
Table I. Products, Yields, and Enantiomeric Excess for Hydroborations of Vinyl Ethers

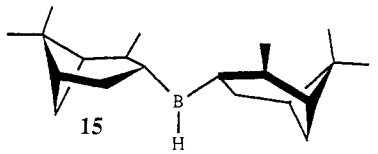
vinyl ether reactant	compd for ee	time, h	yield: NMR, isol	ee	confign
1-methoxycyclohexene	**9a**	8	–, 44	37.5 ± 1.6	*R,R*
1-(benzyloxy)cyclohexene	**12**	6	84, –	24.3 ± 0.8	*R,R*
1-(trimethylsiloxy)cyclohexene	**12**	1	–, 31	27.6 ± 0.5	*R,R*
1-methoxycyclopentene	**10a**	8	–, 66	28.9 ± 0.1	
1-(benzyloxy)cyclopentene	**10b**	14.5	88, –	23.2 ± 1.7	
2-(benzyloxy)-1-heptene	**11b**	20	29, –	5.4	*S*
		0.5	58, –		*S*
2-(diphenylmethoxy)-1-heptene	**11c**	20	77, 46	17.8	*R*

Scheme II



Results

In order to provide a data base for comparison with anticipated more elaborate studies, we have carried out the chiral hydroborations shown in Scheme II. This scheme depicts the reaction of vinyl ethers **6–8** to give the alkoxy diols **9–11**, which are convertible to the diols **12–14** when R is cleavable. We used benzyl and diphenylmethyl vinyl ethers as examples of bulky, cleavable OR groups. In this connection, we note that some exploration of the effect of benzyl and trityl groups protecting the hydroxyl group of crotyl alcohol during hydroborations has been made.[7] Here primary alkoxy secondary β-borane intermediates are formed, whereas for our study the reverse stereochemistry is present. In our study we used Brown's crystalline diisopinocampheylborane, Ipc_2BH, **15**, as the hydroborating agent. Brown has reported the hydroboration of one class of vinyl ethers, dihydropyrans and dihydrofurans, with this reagent.[8]



Syntheses of Vinyl Ethers. The cyclic benzyl ethers **6b** and **7b** were prepared from the ketals as described in the literature.[9] In the case of the aliphatic ethers, we investigated a preparation by ester methylenation. We prepared benzyl and diphenylcarbinyl esters from hexanoic acid and the appropriate alcohols by using dicyclohexylcarbodiimide.[10] This procedure failed for the preparation of triphenylmethyl hexanoate. Success was achieved by using the esterification method of Noyori.[11] The procedure utilizes equimolar amounts of a trimethylsilylated carboxylic acid and trimethyl(trityloxy)silane with 1 mol % of trimethylsilyl trifluoromethanesulfonate.

The esters of hexanoic acid were subjected to carbonyl methylenation using the Tebbe reagent, $Cp_2TiCH_2(Cl)$-$AlMe_2$.[12] We were able to prepare the benzyl and diphenylmethyl vinyl ethers, **8b** and **8c**. The attempted preparation of the particularly interesting triphenylmethyl ether from trityl heptanoate, however, led only to the isolation of triphenylcarbinol. In one attempt, there was NMR evidence that a small amount of vinyl ether had been formed, but the result was not repeatable.

Hydroborations and Determination of Configurations. The results of our hydroborations of the vinyl ethers (Scheme II) using a suspension of Ipc_2BH in THF are given in Table I. The determination of enantiomer ratios using chiral NMR shift reagents is described in the accompanying paper.[13]

Because we suspected that some of our hydroborations involved $IpcBH_2$ formed by dissociation of Ipc_2BH, we prepared $IpcBH_2$ by the method described in the literature[14] and allowed it to react with 1-methoxycylcopentene, **7a**. No 2-methoxycyclopentanol was formed. Instead, cyclopentanol was formed, presumably from elimination of the intermediate alkoxyborane to cyclopentene followed by hydroboration. We comment on this observation in the Discussion section of this paper.

In order to assign the configuration of *trans*-1,2-cyclohexanediol obtained from hydroboration of the vinyl ethers followed by cleavage of the benzyl group (Scheme II), we prepared a sample of (*R,R*)-1,2-cyclohexanediol by hydrolysis of *trans*-1,2-cyclohexanediol diacetate in the presence of pig liver esterase.[15] The NMR spectra of the diols in the presence of a chiral shift reagent were compared. The configurations of 1,2-heptanediol samples from cleavages of the alkoxy alcohols **11b** and **11c** were assigned by comparison of the sign of optical rotation with that reported for (*S*)-(+)-1,2-heptanediol synthesized from D-mannitol.[2]

Discussion

Although the cyclic vinyl ethers were not structures of interest for our projected synthetic needs, we began our studies with them because their synthesis had been reported, and because an anticipated side reaction in the hydroboration of acyclic vinyl ethers, syn elimination of β-alkoxyborane intermediates,[16–19] would not be a com-

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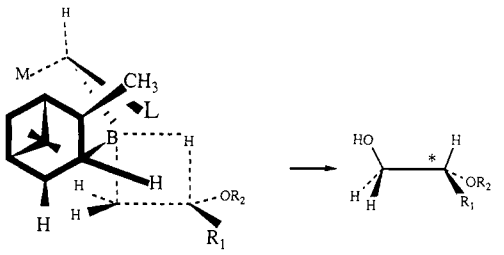
Scheme III



plication. (Anti elimination was still possible.) The yields of alkoxy alcohols that we obtained (Table I) are indicative of the extent to which the elimination reactions were averted.

When we turned to the hydroborations in the acyclic series, some substantial yields were again obtained (Table I). It is particularly interesting that yields for the hydroboration of 2-(diphenylmethoxy)-1-heptene were above 60% (NMR data) whether the completed reaction was allowed to stand for 1 or 20 h. In both cases the borane had dissolved, indicating that reaction had occurred, soon after the mixing was brought to room temperature. Accordingly, in this case *the β-alkoxyborane was substantially stable*, once formed. Whether this stability occurs only when a bulky RO group and a bulky borane group are present to disfavor syn elimination remains to be investigated.

Another factor that could be anticipated to influence the hydroborations of our study was the possibility of prior dissociation of Ipc_2BH to $IpcBH_2$ and pinene. The presence of unreacted pinene in equilibrium with solid Ipc_2BH was noted by Brown and Moerikofer.[20] The hydroborations (using Ipc_2BH) of *trans*-alkenes,[21] trisubstituted alkenes,[20] and a 1,1-disubstituted alkene having a bulky substituent[22] appear to occur, at least in part, by prior dissociation. The resulting products exhibit only moderate values of the enantiomeric excess, in contrast with those from the less sterically demanding *cis*-alkenes[23] and dihydrofurans.[8]

In contrast with the dihydrofurans,[8] the vinyl ethers of our study (Scheme II) are oxygen analogues of trisubstituted or terminally disubstituted alkenes, suggesting the possibility of complications arising from prior dissociation of Ipc_2BH. In possible support for prior dissociation was the observation of some pinene in some of our reaction mixtures. On the other hand, as was mentioned earlier, preprepared $IpcBH_2$ did not give 2-methoxycyclopentanol from 1-methoxycyclopentene. The possible reactions of other hydroborating species, including the hydrogen-bridged mixed dimer and the intermediate boranes, R-(Ipc)BH, further complicate the picture. Accordingly, the nature of the hydroborating agent in our reactions remains to be clarified.

Since several hydroborating species could have been present, and since our ee values are low, we give a minimal mechanistic discussion involving only one aspect of our results. We note that the interesting reversal of configuration that occurs upon increasing the number of phenyl groups in the aliphatic vinyl ethers **8b** and **8c** is explainable by a model developed by Houk et al. for interpreting hydroborations by Ipc_2BH.[24] According to the Houk model, the preferred approach of a vinyl ether to Ipc_2BH (from (+)-pinene) when R_2O is smaller than R_1 is that shown in Scheme III. Here L, the largest group of the rear pinane moiety, interacts with the small R_2O group. Our configurations (for (−)-pinene reactant) are those predictable from the model if $PhCH_2O$ is smaller than R_1, but Ph_2CHO is larger than R_1.

The examination of models for the transition state for hydroboration when the R_2O group is Ph_3CO shows that interactions with Ipc_2BH might be substantially larger than when R_2O is Ph_2CH. Although we did not achieve the synthesis of this desired ether in this phase of our study, the demonstration that chiral hydroboration is possible for a vinyl ether as bulky as the diphenylmethyl ether encourages further work.

Experimental Section

Materials. Tetrahydrofuran was distilled from sodium benzophenone ketyl, methylene chloride from phosphorus pentoxide, hexamethylphosphoric triamide and tetramethylethylenediamine from CaH_2, and pyridine from Na metal. (−)-α-Pinene (98%) was obtained from Aldrich Chemical Co., distilled from lithium aluminum hydride (potential explosion hazard?), and stored under nitrogen. Chiral lanthanide shift reagents were obtained from Aldrich.

Chromatography and Distillation. Flash column chromatography was performed by using E. Merck silica gel 60 (230–400 ASTM mesh) or neutral alumina (Brockman activity 1, 80–200 mesh) supplied by Fisher Scientific Co. Analytical thin-layer chromatography was performed with Analtech silica gel G glass backed plates. High-performance liquid chromatography was carried out on a Waters 6000-A instrument equipped with a U6K injection system, R-401 refractive index detector, 440 UV detector, and RCM-100 radial compression module. Silica gel, 5 μm, or C-18 reverse phase, 5 μm, was used. A Nester-Faust annular still (NFA-100) was used for spinning band distillations.

NMR and Optical Rotation. All NMR spectra were recorded on a Bruker AM 300 spectrometer and sometimes replotted on an Aspect-1000 data station. Except as mentioned, NMR spectra were recorded at a high signal-to-noise ratio and appear to show negligible amounts of impurities. Chemical shifts are reported with respect to tetramethylsilane, based on the assumption that the chemical shift difference between $CHCl_3$ in $CDCl_3$ and TMS is 7.24. Shifts are reported to ±0.001, since reproducibilities are better than 0.01 in moderately dilute solutions. NMR data are given for various known compounds whose NMR spectra at 300 MHz were not available. Optical rotations were measured on a Perkin-Elmer 243B polarimeter using a 10-cm, 1-mL cell.

Preparation of 1-(Benzyloxy)cyclohexene (6b). The preparation reported by House et al.[9] was repeated. The ketal of cyclohexanone was prepared as described[25] by Noyori et al. The pyrolysis of 2.00 g of the ketal in the presence of ammonium dihydrogen phosphate in a Kugelrohr, followed by flash chromatography on neutral alumina, gave 28% of **6b**: ^1H NMR δ 7.29 (m, 5 H), 4.714, (t, 1 H), 4.696 (s, 2 H), 2.803 (m, 4 H), 1.552 (m, 2 H).

Preparation of 1-Methoxycyclopentene (7a). A procedure from the literature was used.[26] Cyclopentanone (10.1 g), trimethyl orthoformate (12.6 g), and *p*-toluenesulfonic acid (0.113 g) were subjected to spinning band distillation after 24 h to give 6.66 g, 57%: 1H NMR δ 4.432 (t, 1 H), 3.578 (s, 3 H), 2.305 (m, 4 H), 1.857 (quartet, 2 H).

Preparation of 1-(Benzyloxy)cyclopentene (7b). A procedure similar to that used for 1-(benzyloxy)cyclohexene was

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employed. The benzyl ketal of cyclopentanone was obtained in 93% yield. Pyrolysis of 2.00 g of the ketal and purification gave the vinyl ether **7b** in 28% yield. (There was some mechanical loss.)

Preparation of Benzyl Hexanoate. The procedure of Hassner and Alexanian[10] gave the ester (58% after flash chromatography) from 1.16 g of hexanoic acid and 1.18 g of benzyl alcohol: ^{1}H NMR δ 7.37 (m, 5 H), 5.10 (s, 2 H), 2.36 (t, 2 H), 1.63 (quintet, 2 H), 1.24 (m, 5 H), 0.87 (t, 3 H).

Preparation of Diphenylmethyl Hexanoate. The procedure used for benzyl hexanoate gave the ester (77% from flash chromatography), starting from hexanoic acid (1.16 g) and benzhydrol (2.03 g): ^{1}H NMR δ 7.22 (m, overlapping $CHCl_3$), 6.870 (s, 1 H), 2.400 (t, 2 H), 1.645 (quintet, 2 H), 1.26 (m, 4 H), 0.852 (t, 3 H).

Preparation of 2-(Benzyloxy)-1-heptene (8b). The preparation was similar to that for 2-(diphenylmethoxy)-1-heptene (below). From 1.25 g of benzyl hexanoate there was obtained 0.55 g (47%) of the vinyl ether, free of impurities by NMR: ^{1}H NMR δ 7.34 (m), 4.724 (s, 2 H), 3.929 (d, J = 1.95), 3.913 (d, J = 1.95), 2.135 (t), 1.53 (m), 1.29 (m), 0.874 (m).

Preparation of 2-(Diphenylmethoxy)-1-heptene (8c). To a 50-mL round-bottomed flask equipped with a septum, stirring bar, and nitrogen-filled balloon were added diphenylmethyl hexanoate (1.56 g, 0.005 73 mol), toluene (6 mL), THF (2 mL), and pyridine (40 mL). The mixture was cooled to −40 °C. Tebbe's reagent,[12] $Cp_2TiCH_2(Cl)AlMe_2$ (2.43 g, 0.008 56 mol), in toluene was added dropwise. The mixture was stirred at −40 °C for 1 h and brought to room temperature for 11 h. The mixture was cooled to −10 °C. NaOH (2 mL of 15%) was added. The mixture was stirred for 60 min, diluted with ether, and filtered with the aid of Celite. Evaporation and flash chromatography gave 1.51 g, 94%, calculated as pure **8c** but containing approximately 18% diphenylmethyl hexanoate by NMR analysis: ^{1}H NMR δ 7.32 (m, overlapping $CDCl_3$), 5.921 (s, 1 H), 3.893 (d, J = 1.9, 1 H), 3.806 (d, J = 1.9, 1 H), 2.166 (t, 2 H), 1.541 (quintet), 1.54 (m), 0.877 (t), plus peaks for diphenylmethyl hexanoate.

Preparation of (+)-Diisopinocampheylborane (15). The preparation reported by Brown and Singaram[19] was repeated, except that 98% (−)-(α)-pinene (7.94 mL, 0.051 mol) was used and a flame-dried Erlenmeyer flask equipped with a stirring bar, septum, and nitrogen balloon was used. Adding dropwise 2.5 mL (0.25 mol) of 10 M borane–methyl sulfide complex, storage in the refrigerator for 20 h, transfer in a dry bag to a flame-dried pressure funnel (Ace Glassware), and washing with ether gave 4.27 g (60%) of the borane.

Hydroboration of 2-(Benzyloxy)-1-heptene (8b). A procedure similar to that for 2-(diphenylmethoxy)-1-heptene (below) gave a crude material whose NMR spectrum with an internal standard indicated a yield of 29% when the reaction mixture was brought to room temperature for 20 h or 64% when the reaction mixture was brought to room temperature for 1 h (Table I). The material was not separable from isopinocampheol by flash chromatography on silica gel. However, HPLC with ethyl acetate–cyclohexane gave a pure sample of the known[27] 2-(benzyloxy)-1-heptanol (**11b**) for NMR: ^{1}H NMR δ 7.292 (m), 4.566 (dd, 2 H), 3.674 (m, 1 H), 3.505 (m, 2 H), 1.564 (m, 2 H), 1.275 (m, 6 H), 0.866 (t, 3 H).

Hydroboration of 2-(Diphenylmethoxy)-1-heptene (8c). To a flame-dried 50-mL round-bottomed flask equipped with a septum, stirring bar, and N_2 balloon were added (in a dry bag) 1.58 g (0.002 78 mol) of freshly prepared crystalline (+)-diisopinocampheylborane dimer and 6 mL of dry THF. To this white suspension, cooled to 0 °C, was added 1.07 g (approximately 0.0038 mol) of the vinyl ether **8c** containing some ester. The suspension became clear within 30 min after warming to room temperature. After 20 h the flask was equipped with a reflux condenser and cooled to 0 °C. Oxidation was effected by the addition of 6 mL (0.018 mol) of 3 M NaOH and 2 mL (0.0195 mol) of 30% H_2O_2. The mixture was warmed to room temperature and stirred for 4 h. An ether extract yielded 3 g of crude material whose NMR spectrum in the presence of an internal standard indicated a yield of 77%. Repeated flash chromatography using ether–hexanes (1:1) was required to remove isopinocampheol. 2-(Diphenylmethoxy)-1-heptanol (**11c**) (0.52 g, 46%) was obtained as a colorless oil free of isopinocampheol: ^{1}H NMR δ 7.293 (m, 10 H), 5.532 (s, 1 H), 3.679 (m, 1 H), 3.513 (m, 2 H), 1.564 (m, 6 H), 0.846 (t, 3 H).

Hydroboration of 1-Methoxycyclohexene (6a). A procedure similar to that for the reaction of 2-(diphenylmethoxy)-1-heptene was used, except that the reaction was done at room temperature for 8 h. The solution became clear in 35 min. From 4.28 g (0.015 mol) of Ipc_2BH and 1.65 g of **6a** there was obtained (by flash chromatography) (hexanes, ether) 0.84 g (44%) of the known[28-30] *trans*-2-methoxycyclohexanol: ^{1}H NMR δ 3.377 (s, 3 H), 3.382 (m, 1 H), 2.914 (m, 1 H), 2.045 (m, 2 H).

Hydroboration of 1-(Benzyloxy)cyclohexene (6b). A procedure similar to that for the reaction of 2-(diphenylmethoxy)-1-heptene was used. From 0.35 g of **6b** there was obtained a 58% yield of 2-(benzyloxy)cyclohexanol (**9b**), measured by NMR analysis with an internal standard. Flash chromatography on silica gel gave pinene (0.12 g) and the known[28,30] **9b** mixed with isopinocampheol. HPLC gave an NMR sample of **9b**: ^{1}H NMR δ 7.291 (m), 4.568 (dd, 2 H), 3.459 (m, 1 H), 3.179 (m, 1 H), 1.693 (m, 2 H), 1.222 (m, 4 H).

Hydroboration of 1-(Trimethylsiloxy)cyclohexene (6c). A procedure similar to that for the reaction of 2-(diphenylmethoxy)-1-heptene was used. The reaction of Ipc_2BH (1.5 g, 0.0026 mol) and **6c** (available from Petrarch Chemical Co.; 0.75 g, 0.0044 mol) gave 0.16 g (31%) of *trans*-1,2-cyclohexanediol, eluted with ether–acetone (7:3): ^{1}H NMR δ 3.310 (m, 4 H), 1.931 (m, 2 H), 1.663 (m, 2 H), 1.226 (4 H); $[\alpha]^{22}_{589}$ −13.40° for 0.0335 g in 1 mL of water.

Hydroboration of 1-Methoxycyclopentene (7a). A procedure similar to that for the reaction of 2-(diphenylmethoxy)-1-heptene was used. The reaction of 3.87 g (0.0137 mol) of Ipc_2BH and 1.41 g (0.0144 mol) of **7a**, 8 h at room temperature, gave the known[28] *trans*-2-methoxycyclopentanol (1.08 g, 66%) from flash chromatography (3:2 hexanes–ether): ^{1}H NMR δ 4.089 (s, 1 H), 3.542 (s, 1 H), 3.330 (s, 3 H), 1.960 (m, 2 H), 1.662 (m, 2 H).

Hydroboration of 1-(Benzyloxy)cyclopentene (7b). A procedure similar to that for the reaction of 2-(diphenylmethoxy)-1-heptene was used. Reaction of 0.23 g of **7b** gave 88% of 2-(benzyloxy)cyclopentanol by NMR analysis. Chromatography on silica gel gave an NMR sample: ^{1}H NMR δ 7.287 (m), 4.535 (dd, 2 H), 4.170 (m, 1 H), 3.741 (m, 1 H), 1.977 (m, 2 H), 1.701 (m, 4 H).

Deprotection and Optical Rotation of 2-(Benzyloxy)-1-heptanol. A procedure similar to that described below for 2-(diphenylmethoxy)-1-heptanol gave 1,2-heptanediol, 99%, $[\alpha]^{24}_{589}$ −0.972°.

Deprotection of 2-(Benzyloxy)cyclohexanol. A procedure similar to that described below for 2-(diphenylmethoxy)-1-heptanol was used. A mixture of 2-(benzyloxy)cyclohexanol (0.119 g, 0.000 58 mol) and isopinocampheol (0.251 g, 0.0163 mol) upon reaction with Na (0.51 g, 0.022 mol) in NH_3 gave crystalline *trans*-1,2-cyclohexanediol, 0.43 g, 63%.

Deprotection and Assignment of Configuration of 2-(Diphenylmethoxy)-1-heptanol. The removal of benzyloxy groups has been described.[31] Ammonia was condensed from a cylinder in a flask containing sodium. The sodium-dried ammonia was distilled into a flask containing 1.09 g (0.0473 mol) of sodium pellets. 2-(Diphenylmethoxy)-1-heptanol (**11c**) (0.52 g, 0.001 74 mol) dissolved in 10 mL of dry THF was added. The solution turned from deep blue to white to deep blue. Ammonium chloride was added until the solution was white. (Some spillage occurred.) Workup with ether–water extraction and flash chromatography gave 0.14 g (61%) of 1,2-heptanediol: ^{1}H NMR δ 3.673 (m, 2 H), 3.410 (m, 1 H), 1.481 (m, 8 H), 0.867 (t, 3 H). The rotation of 0.103 g in ethanol (1 mL) was measured, $[\alpha]^{23.5}_{589}$ +2.903°. For the preparation of the *S*-(−) isomer and references to earlier preparations, see ref 2.

Preparation of Partially Resolved (*R*,*R*)-*trans*-2-Methoxycyclohexanol. A flame-dried, 50-mL flask equipped with

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a septum, stirring bar, and N_2 balloon was charged with 10 mL of dry tetrahydrofuran and 1.45 mL (0.002 32 mol) of *n*-butyllithium, 1.6 M, in hexanes. To this mixture was added 0.265 g (0.002 28 mol) of partially resolved (−)-(*R,R*)-*trans*-1,2-cyclohexanediol in 15 mL of dry tetrahydrofuran. (The diol had been obtained by chiral hydroboration–oxidation of 1-(trimethylsiloxy)cyclohexene.) After 30 min, iodomethane (0.15 mL, 0.002 41 mol) was added dropwise over 30 min. Then 5 mL of hexamethylphosphoric triamide was added in one portion. The mixture was stirred overnight and quenched by the addition of aqueous KOH. After 4 h, isolation by ether extraction and flash chromatography on silica gel gave 0.02 g (7%) of the title compound, needed for configurational assignment of the product of hydroboration of 1-methoxycyclohexene.

Registry No. **6a**, 931-57-7; **6b**, 29494-42-6; **6c**, 6651-36-1; **7a**, 1072-59-9; **7b**, 113548-17-7; **8b**, 113548-19-9; **8c**, 113548-20-2; **9a**, 113625-71-1; **9b**, 85761-38-2; **10a**, 113625-72-2; **10b**, 113625-73-3; **11b**, 113548-21-3; **11c**, 113548-22-4; **12**, 1072-86-2; (*S*)-**14**, 61229-00-3; (*R*)-**14**, 78843-64-8; **15** (dimer), 16997-72-1; $NH_4PO_4H_2$, 7722-76-1; $C_5H_{11}CO_2CH_2Ph$, 6938-45-0; $C_5H_{11}CO_2CHPh_2$, 113548-18-8; Ph_2CHOH, 91-01-0; $Cp_2TiCH_2(Cl)AlMe_2$, 67719-69-1; cyclohexanone dibenzyl ketal, 29494-49-3; cyclopentanone dibenzyl ketal, 2882-93-1; (+)-isopinocampheol, 24041-60-9.

Methodology for the Analysis of Products from Asymmetric Syntheses Using Chiral NMR Shift Reagents. Relative Complexation Constants of Enantiomers[1]

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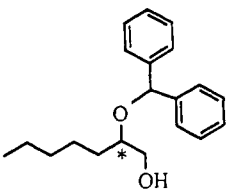
The enantiomeric excess (ee) of β-alkoxy alcohols and diols from asymmetric hydroboration of vinyl ethers was determined by 300-MHz NMR using chiral shift reagents. The use of Gaussian line narrowing and base-line correction to facilitate analyses is illustrated. Computer-assisted determination of the origins of shifted peaks with the aid of a calculated apparent complexation constant, *K*, is illustrated. The mathematics for simultaneous complexation of enantiomers having different *K* values is derived. For the first time, the contribution of differential complexation in NMR chiral shift studies was determined. For the case studied, both enantiomers were complexed to similar extents.

In the course of studies of the hydroboration–oxidation of vinyl ethers to give partially resolved β-alkoxy alcohols,[2] we became interested in the interpretation and optimal utilization of the NMR analyses obtained by using chiral Eu and Yb NMR shift reagents. In this paper we first illustrate some advantageous manipulations of the NMR data both at the console of the spectrometer or plotting station and by analysis using a personal computer. This portion of the paper deals with the application of known methodology and principles as they relate to modern instrumentation and to the needs of chemists involved in asymmetric synthesis.

We also report here the derivation of the mathematics required to separate the effects of differential complexation of enantiomers from the effects of differential shifting of NMR peaks in diastereomeric one-to-one complexes with NMR shift reagents. These separate effects were recognized, but not quantitatively evaluated, when chiral NMR shift reagents were first studied.[3] In a preliminary application of the derivation, we used a computerized, iterative procedure to determine the apparent *K* values for complexation of enantiomers obtained by asymmetric hydroboration of a vinyl ether. The term "apparent *K* values" refers here to equilibrium constants applicable to the widely employed one-to-one complex model.[4] Evidence for other types of complexes appears in the literature. However, all calculational efforts in the area may be regarded as simplified models when the full complexity of the systems is considered. For example, the possible existence of eight geometrical isomers has been discussed for one type of complex.[5]

Assessing Enantiomer Ratios. The spectra obtained from 14 additions of a solution of Yb(hfc)$_3$, tris[3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato]ytterbium(III) derivative, to an NMR tube containing 2-(diphenylmethoxy)-1-heptanol (**11c**) (same numbering as in



11c

the accompanying paper) appeared to constitute an unusually favorable case for assessing the precision of analysis for enantiomer ratios. Examination of the spectra showed

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