benzene), a value which corresponds to ~100% ee.

The combined washings were collected, and excess methanol was added. Oxidation as before yielded isopinocampheol with $[\alpha]^{25}_D$ −30.2° (c 1.2, benzene), a value which corresponds to 84.6% ee. This result therefore indicates that the minor isomer has accumulated in the solution.

In another reaction, 2IpcBH$_2$·TMED was prepared on a 250-mmol scale, and the dehydroborated α-pinene was recovered from the washings as shown below. The volatiles (Et_2O and pentane) were removed, and the residue was then steam distilled. α-Pinene (49.5 mL, 95%) was collected. This was further purified by distillation over $LiAlH_4$ to yield 45.8 mL (88%) of pure α-pinene: $[\alpha]^{23}_D$ +47.6° (neat), ~93% ee.

Preparation of 3 from 6. For liberation of the free borane **3**, 14.6 g of **6** (35 mmol) was dissolved in 50 mL of THF, and 8.6 mL (70 mmol) of BF_3·OEt_2 was added with constant stirring. After 1.25 h at 25 °C, the precipitation of 2BF_3·TMED was complete. The solution containing free borane **3** was removed from the slurry of 2BF_3·TMED by filtration as before. The solid 2BF_3·TMED was washed with dry, ice-cold THF (3 × 9 mL), and the washings were transferred to the main solution. The filtrate was analyzed for IpcBH$_2$ by hydrolysis. The recovery of IpcBH$_2$ is 80–84%.

Preparation of 6 from 2ThxBH$_2$·TMED. Neat ThxBH$_2$ was prepared as before by adding 1.2 mL (10 mmol) of TME to 1.0 mL of 10 M (10 mmol) BH_3·SMe_2 at 25 °C for 0.5 h. To this reaction mixture was added 0.75 mL (5 mmol) of TMED followed by the addition of 2.0 mL of Et_2O, thus providing a 1.0 M solution of 2ThxBH$_2$·TMED in Et_2O. The Et_2O solvent was refluxed, and 1.6 mL (10 mmol) of (+)-α-pinene was added. The reaction mixture was refluxed for 6 h. The volatiles were then removed under aspirator vacuum (12 mm) to yield **6** in 95% isolated yield. This is then crystallized from Et_2O to yield pure **6**, mp 140–141 °C.

Preparation of 3 by the Equilibration of 1:1 α-Pinene and BH_3·THF. The reaction was carried out in a 100-mL flask. The flask was charged with 22.03 mL of 2.27 M (50 mmol) BH_3·THF and 41.4 mL of THF to make the resulting reaction mixture 0.7 M with respect to borane. (+)-α-Pinene (8.0 mL) was then added, and the reaction mixture was stirred for ~96 h at 25 °C. During this time the reaction attained equilibrium, and the equilibrium mixture contained 91% IpcBH$_2$ and 4.5% each of Ipc$_2$BH and BH_3·THF. THF was removed under vacuum and replaced by 30 mL of pentane. Addition of 0.17 mL (1.1 mmol) of TMED precipitated BH_3 as 2BH_3·TMED in 0.75 h, which was removed from the supernatant solution by filtration as before. The 2BH_3·TMED was washed with portions (2 × 5 mL) of cold pentane, and the washings were added to the main solution. Thus a solution of IpcBH$_2$ (>95%) in THF was obtained.

Acknowledgment. This investigation was supported by Grant 2 R01 GM 10937-9 from the National Institutes of Health. We are deeply indebted to Dr. E. Klein of the Dragoco Co., Holzminden, West Germany, for a generous gift of high-purity α-pinene.

Registry No. 1, 56118-59-3; 2, 64234-28-2; 3, 64234-27-1; 4, 67826-91-9; 5, 67826-89-5; 6, 67826-92-0; TMED, 110-18-9; BH_3·THF, 14044-65-6; BH_3·SMe_2, 13292-87-0; Ipc$_2$BH, 21947-87-5; 2ThxBH$_2$·TMED, 67826-90-8; (+)-α-pinene, 7785-70-8; thexylborane, 3688-24-2; isopinocampheol, 27779-29-9.

Hydroboration. 62. Monoisopinocampheylborane, an Excellent Chiral Hydroborating Agent for Trans-Disubstituted and Trisubstituted Alkenes. Evidence for a Strong Steric Dependence in Such Asymmetric Hydroborations

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Received April 9, 1982

Monoisopinocampheylborane (IpcBH$_2$), the first monoalkylborane chiral hydroborating agent, is capable of reacting with olefins of varying structural and steric requirements to produce, in most cases, clean dialkylboranes. IpcBH$_2$ achieves the asymmetric hydroboration of trans-disubstituted and trisubstituted olefins with exceptionally high asymmetric induction. The product alcohols, produced by oxidation of the intermediate organoboranes, exhibit enantiomeric purities in the range of 53–100% ee and reveal the same absolute configuration. Enantiomeric purities of the products increase with increasing steric requirements of the alkyl or phenyl substituent in the trans-disubstituted or trisubstituted alkene.

Organoboranes are clearly one of the most versatile organometallic intermediates for organic synthesis.[1] The stereospecificity and regioselectivity provided by monoalkyl- and dialkylboranes in the hydroboration of olefins is remarkable. This property, coupled with an asymmetric attack on the enantiotopic face of prochiral olefin by a chiral hydroborating agent makes this reaction a most valuable one for asymmetric synthesis. In fact, in 1961, the chiral hydroborating agent diisopinocampheylborane (Ipc$_2$BH, 1) marked the beginning of a practical, nonenzymatic asymmetric synthesis.[2] Prior to this time, asymmetric syntheses had been very inefficient, with the excess of one enantiomer over the other produced in the known asymmetric syntheses being generally quite small and hardly of practical utility.

Diisopinocampheylborane is currently one of the most versatile chiral reagents readily available for laboratory use.[3] It is readily prepared by the hydroboration of α-pinene with diborane,[4] BH_3·THF,[5] or BH_3·SMe_2.[6] The

(1) (a) Brown, H. C. "Boranes in Organic Chemistry"; Cornell University Press: Ithaca, NY, 1972. (b) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. "Organic Syntheses via Boranes"; Wiley-Interscience: New York, 1975. (c) Pasto, D. J. In "Boron Hydride Chemistry"; Mutterties, E. L., Ed.; Academic Press: New York, 1975. (d) Pelter, A.; Smith, K. In "Comprehensive Organic Chemistry"; Barton, D. H. R.; Ollis, W. D.; Pergamon Press: Oxford, 1979; Vol. 3.

(2) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 486.

(3) For a recent review on "Asymmetric Syntheses via Chiral Organoborane Reagents", see: Brown, H. C.; Jadhav, P. K.; Mandal, A. K. *Tetrahedron* **1981**, *37*, 3547.

(4) Brown, H. C.; Ayyangar, N. R.; Zweifel, G. *J. Am. Chem. Soc.* **1964**, *86*, 397.

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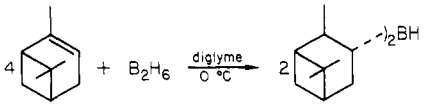
hydroboration of α-pinene proceeds to the dialkylborane stage and does not continue to the trialkylborane stage, even in the presence of excess α-pinene (eq 1). The

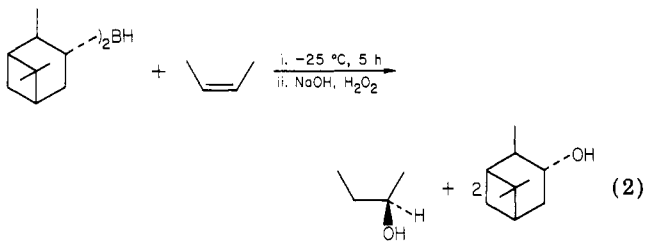


(1)

1

successful applications of organoboranes in synthesis require their ready availability. Fortunately, both (+)- and (−)-α-pinenes are readily available. Indeed, it is the most abundant monoterpene in the world. Therefore, numerous applications of this reagent have appeared in the literature over the past 20 years. It has been used for the reduction of ketones and 1-deuterioaldehydes to the corresponding chiral secondary alcohols and chiral monodeuterio primary alcohols.[3] The kinetic resolution of alkenes, dienes, and allenes by this valuable reagent has been extensively studied.[3] Ipc_2BH has been applied for the asymmetric hydroboration of prochiral olefins to provide chiral products such as alcohols, amines, halides, hydrocarbons, and ketones.[3] It has been also applied for the asymmetric synthesis of natural products such as prostaglandin $F_{2\alpha}$,[3] loganin (an important building block in the plant world),[3] and the carotenoid zeaxanthin.[7] A major advantage of Ipc_2BH is the ready availability of both enantiomers of α-pinene. Consequently, chiral centers of opposite configuration can be generated by using Ipc_2BH derived from the appropriate antipode of α-pinene.

Ipc_2BH is an excellent chiral hydroborating agent for cis-disubstituted alkenes such as *cis*-2-butene and *cis*-3-hexene. Thus, *cis*-2-butene, on hydroboration with Ipc_2BH followed by oxidation with alkaline hydrogen peroxide, provides 2-butanol in 98.4% enantiomeric purity[5] (eq 2).



(2)

98.4% ee

However, the reactions of Ipc_2BH with relatively more hindered olefins such as trans-disubstituted and trisubstituted alkenes, are more sluggish, are mechanistically complicated, and occur with partial displacement of α-pinene from the reagent.[8] In such cases, the product alcohols are obtained in much lower enantiomeric purities, in the range of only 14–22% ee.

It appeared desirable to prepare a new chiral hydroborating agent with steric requirements lower than those of Ipc_2BH to overcome these difficulties. The immediate solution would have been a monoalkylborane derived from α-pinene. Unfortunately, under normal conditions the hydroboration of α-pinene cannot be stopped at the monalkyborane stage. Indeed, the first report of a monoalkylborane chiral hydroborating agent came only 15 years after the discovery of Ipc_2BH in 1961. The limiting factor was the inability to stop the hydroboration at the desired monoalkylborane stage. The discovery of new organoborane reagents, new methods for their synthesis, and new applications made possible the first synthesis of monoisopinocampheylborane ($IpcBH_2$) by indirect hydroboration procedures.

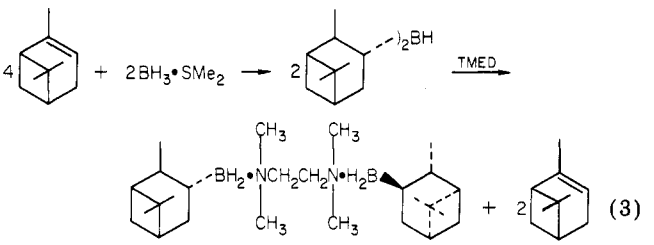
This reagent was prepared for the first time via its triethylamine complex and proved very useful for the chiral hydroboration of trisubstituted olefins.[9] Therefore, several syntheses were explored to provide a convenient preparation of this desirable reagent. The chemistry uncovered during the development of these syntheses is interesting. A detailed account of the different syntheses of $IpcBH_2$ developed is given in the preceding paper.[10]

In the early exploration of $IpcBH_2$, we were content with the hydroboration results with only three olefins, viz., 2-methyl-2-butene, 1-methylcyclopentene, and 1-methylcyclohexene. With the avialability of simple, convenient syntheses of optically *pure* $IpcBH_2$,[11] it became desirable to establish the degree of asymmetric induction with a wide variety of olefins. Consequently, we undertook a systematic investigation to determine the asymmetric hydroboration characteristics of $IpcBH_2$ with olefins of varying structural and steric requirements. In our search we observed that $IpcBH_2$ hydroborates both trans-disubstituted and trisubstituted alkenes, olefin classes which could not be handled by Ipc_2BH, providing product alcohols, after oxidation, in enantiomeric purities ranging from 50% to 100%.

A portion of our results has appeared in the form of preliminary communications.[12,13] We now describe in full the results of our study on the asymmetric hydroboration characteristics of monoisopinocampheylborane.

Results and Discussion

Method of Preparation of $IpcBH_2$. Among the several methods of synthesis, we prepared $IpcBH_2$ via its bis adduct with TMED, $2IpcBH_2 \cdot TMED$[10,11] (eq 3). It appears to be the most simple, convenient preparation of those explored. It allows one to use the readily available $BH_3 \cdot SMe_2$ complex. The crystalline adduct was isolated and washed with pentane in the same reaction flask by using the double-ended needle technique.[1b] This modification from the original procedure avoids the use of a centrifuge and permits the preparation of $2IpcBH_2 \cdot TMED$ on a large scale. The generation of $IpcBH_2$ from the adduct is achieved by treatment with $BF_3 \cdot OEt_2$[11] (eq 4).



(3)

$2IpcBH_2 \cdot TMED$

$$2IpcBH_2 \cdot TMED + 2BF_3 \cdot OEt_2 \rightarrow 2IpcBH_2 + 2Et_2O + 2BF_3 \cdot TMED\downarrow \quad (4)$$

$IpcBH_2$ is conveniently separated from solid $2BF_3 \cdot TMED$ by filtration through a filter chamber, and the molarity

(5) Brown, H. C.; Yoon, N. M. *Isr. J. Chem.* **1977**, *15*, 12.
(6) Brown, H. C.; Desai, M. C.; Jadhav, P. K. *J. Org. Chem.*, preceding paper in this issue.
(7) Rüttimann, A.; Mayer, H. *Helv. Chim. Acta* **1980**, *63*, 1456.
(8) Brown, H. C.; Ayyangar, N. R.; Zweifel, G. *J. Am. Chem. Soc.* **1964**, *86*, 1071.
(9) Brown, H. C.; Yoon, N. M. *J. Am. Chem. Soc.* **1977**, *99*, 5514.
(10) Brown, H. C.; Mandal, A. K.; Yoon, N. M.; Singaram, B.; Schwier, J. R.; Jadhav, P. K. *J. Org. Chem.* preceding paper in this issue.
(11) Brown, H. C.; Schwier, J. R.; Singaram, B. *J. Org. Chem.* **1978**, *43*, 4395.
(12) Mandal, A. K.; Jadhav, P. K.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 3543.
(13) Brown, H. C.; Jadhav, P. K. *J. Org. Chem.* **1981**, *46*, 5047.

Table I. Reactions of Representative Olefins with Monoisopinocampheylborane ($IpcBH_2$) in the Molar Ratio of 1:1[a]

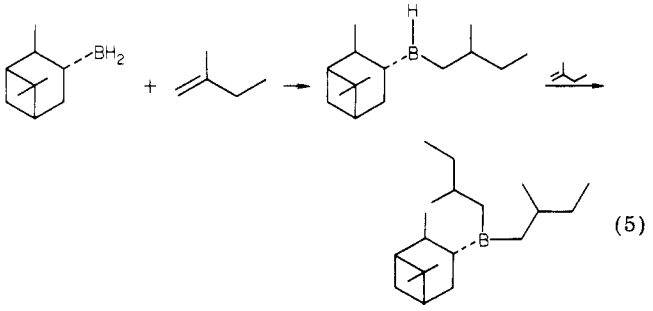
olefin	temp, °C	time, h	% yield $IpcBR_2$	$IpcBHR$	$IpcBH_2$	RBH_2
2-methyl-1-butene	−25	4	24	52	24	0
trans-2-butene	−25	9	0	93	7	0
2-methyl-2-butene	−25	9	0	96	4	0
2-methyl-2-pentene	−25	9	0	95	3	trace
1-methylcyclopentene	−25	9	0	95	5	trace
1-ethylcyclopentene	−25	9	0	95	5	trace
(*E*)-3-phenyl-2-pentene	−25	48	0	85	13	2
1-phenylcyclopentene	−25	24	0	92	8	trace
1-phenylcyclohexene	0	168	0	69	19	12

[a] $IpcBR_2$ based on ^{11}B NMR examination. $IpcBHR$ = ROH-RBH_2. RBH_2 = α-pinene eliminated. $IpcBH_2$ = olefin unreacted and/or ^1H NMR examination of *B*-methoxyboranes.

of the solution is determined by hydride estimation.[1b] The most unique advantage of this preparation over the other is its production of 100% enantiomerically pure $IpcBH_2$, utilizing optically less pure α-pinene. For the present study, we prepared and used $IpcBH_2$ of 100% ee utilizing (+)-α-pinene of 95% ee.

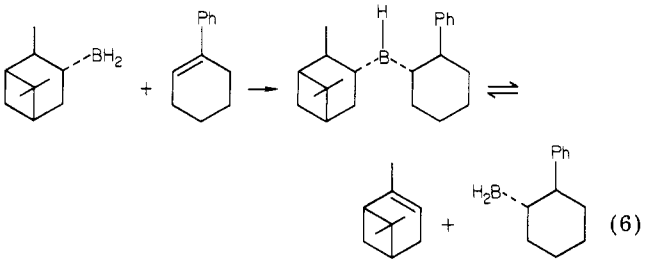
Hydroboration of Representative Olefins with $IpcBH_2$. In all, nine representative olefins of different steric requirements were selected for this study. Each olefin was hydroborated with an equimolar quantity of $IpcBH_2$ (0.7 M in olefin and $IpcBH_2$). The reaction was monitored by quenching aliquots in methanol, followed by examination of the ^{11}B NMR of the sample. The structure of the reaction intermediate was determined by a combination of ^{11}B NMR, ^1H NMR of the *B*-methoxyboranes, and GLC analysis of the oxidized reaction mixture. The ^1H NMR examination of the methanolyzed product, following evaporation of THF and methanol [25 °C (15 mm), 1–2 h], provides a convenient means for determining the quantities of monomethoxy- and dimethoxyboranes.[14] In all cases examined, the methoxy protons of monomethoxydialkylborane appear downfield (δ 3.65–3.85) relative to those of dimethoxymonoalkylboranes (δ 3.5–3.6). The quantitative determination of the product alcohol, unreacted olefin, and the α-pinene eliminated was achieved by GLC analysis of the oxidized reaction mixture in the presence of an internal standard. The amount of unreacted olefin corresponds to the amount of $IpcBH_2$ in the reaction mixture. Similarly, the amount of α-pinene eliminated corresponds to the amount of RBH_2. The results of our study are summarized in Table I.

The formation of trialkylborane was observed only in the case of 2-methyl-1-butene and may be due to the competitive hydroboration of 2-methyl-1-butene with the intermediate dialkylborane (eq 5). In the case of (*E*)-3-



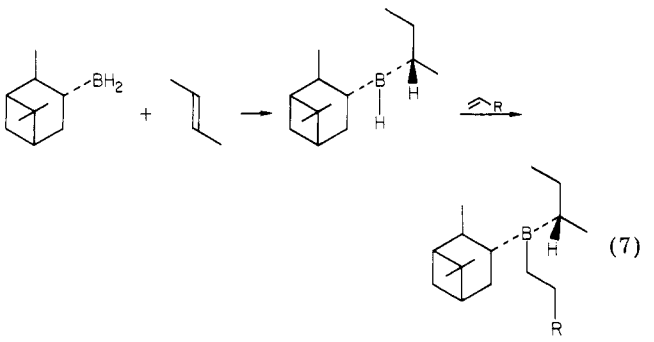
(5)

phenyl-2-pentene, a considerable amount of unreacted olefin was observed, probably because of insufficient reaction time for the relatively slow reaction. The reaction of 1-phenylcyclohexene with $IpcBH_2$ was very sluggish at −25 °C. Therefore, it was carried out at 0 °C. Even at 0 °C, it took 7 days for 80% completion. This was the only case where the elimination of a considerable amount of α-pinene (12%) was noted (eq 6).



(6)

In most cases the reaction intermediates are clean dialkylboranes, indicating that the reaction of $IpcBH_2$ with the majority of olefins proceeds smoothly to provide the desired reaction intermediates. These intermediates may be useful ragents for a second hydroboration to provide synthetically useful trialkylboranes (eq 7). Currently we



(7)

are exploring the synthesis of such mixed trialkylboranes and their utility for the synthesis of other chiral products.

Hydroboration of Representative Examples from Major Classes of Olefins with $IpcBH_2$. One example from each of the four major classes of olefin (2-alkyl-1-alkene, *cis*-alkenes, *trans*-alkenes, and trisubstituted alkenes) was selected for initial study of the asymmetric hydroboration characteristics of $IpcBH_2$. Each olefin selected is characterized by possessing the most simple structure and least hindered nature from that particular class. All of the olefins are prochiral in character. Each olefin was hydroborated with $IpcBH_2$ in the molar ratio of 1:1 at −25 °C. The alkaline hydrogen peroxide oxidation of the methanolyzed reaction mixture provided a mixture of the desired alcohol and isopinocampheol. The product alcohols were readily separated from isopinocampheol by simple distillation. The final purification (GLC purity >99.9%) was achieved by preparative GLC. The optical purity was determined by measuring the rotation of a

(14) Brown, H. C.; Negishi, E.; Katz, J.-J. *J. Am. Chem. Soc.* **1975**, *97*, 2791.

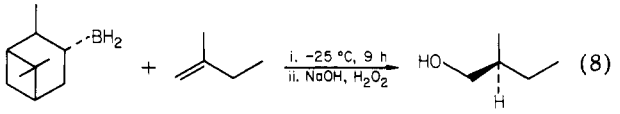
Table II. Asymmetric Hydroboration Results of Representative Examples from Various Classes of Olefins with Monoisopinocampheylborane ($IpcBH_2$)[a]

olefin	product alcohols: alcohol[e]	% yield (isolated)	$[\alpha]^{23}_D$, deg	% ee
2-methyl-1-butene	2-methyl-1-butanol	76	−0.088 (neat)	1.5[b]
cis-2-butene	2-butanol	67	+3.3 (neat)	24[c]
trans-2-butene	2-butanol	73	+9.8 (neat)	73[c]
2-methyl-2-butene	3-methyl-2-butanol	75	+2.65 (neat)	53[d]

[a] The reactions were carried out on a 50-mmol scale in the molar ratio of 1:1. [b] Based on maximum rotation $[\alpha]^{27}_D$ −5.9° (neat): Whitmore, F. C.; Olewine, J. H. *J. Am. Chem. Soc.* **1938**, *60*, 2569. [c] Based on maximum rotation $[\alpha]^{25}_D$ −13.5° (neat): Leroux, P. J.; Lucas, H. J. *Ibid.* **1951**, *73*, 41. [d] Based on maximum rotation α^{27}_D +8.12° (l = 2, neat): Sanderson, W. A.; Mosher, H. S. *Ibid.* **1966**, *88*, 4185. [e] The configuration is *S* in all cases.

chemically pure sample and comparing it with the maximum reported rotation.[15] The results of our study are summarized in Table II.

Thus hydroboration of 2-methyl-1-butene with $IpcBH_2$, followed by oxidation, provided 2-methyl-1-butanol in only 1.5% ee (eq 8). Similar treatment of *cis*-2-butene provided



(8)

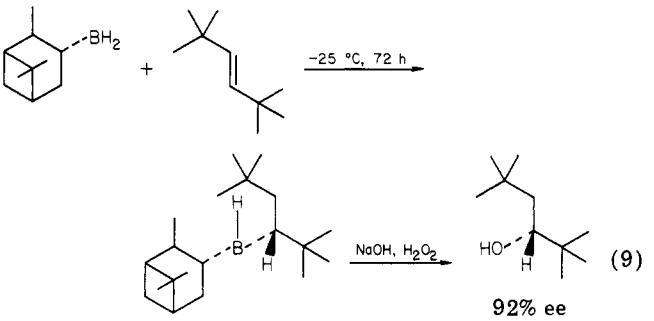
1.5% ee

2-butanol in 24% ee. The results indicate that $IpcBH_2$ fails to give good asymmetric induction in case of 2-methyl-1-alkenes and cis-disubstituted olefins. Because of the unsatisfactory results, no additional examples from the least hindered two major classes of olefins were studied. It may be pertinent to mention here that Ipc_2BH gives a more satisfactory result in the case of 2-methyl-1-alkene (21% ee) and achieves excellent asymmetric induction in the case of *cis*-2-butene (98.4% ee).

In comparison to Ipc_2BH, the hydroboration of *trans*-2-butene and 2-methyl-2-butene with $IpcBH_2$ proceeded cleanly, without any displacement of α-pinene from the reagent. The enantiomeric purities of 2-butanol and 3-methyl-2-butanol are 73% and 53%, respectively. These highly gratifying results encouraged us to study these two classes of alkenes in greater detail. Accordingly, we selected several olefins of different structural and steric requirements from two classes.

Hydroboration of Representative Trans-Disubstituted Olefins with $IpcBH_2$. In all eight olefins were selected for this study. The trans-disubstituted olefins were further arranged into two subclasses, viz., symmetrical and unsymmetrical. Four examples with increasing steric requirements belonged to each subclass. The hydroboration of *trans*-2-butene and *trans*-3-hexene with $IpcBH_2$ was complete within 9 h at −25 °C. In both cases, the intermediate dialkylboranes precipitated within 0.5 h of reaction time. The product alchols, obtained following the alkaline hydrogen peroxide oxidation of the methanolyzed reaction mixtures, were readily separated from isopinocampheol by simple distillation. The chemically pure samples were obtained by purification through preparative GLC. The enantiomeric purities of 2-butanol and 3-hexanol are found to be 73% and 75% by comparison of their rotations with the maximum value reported.

The hydroboration of *trans*-2,2,5,5-tetramethyl-3-hexene was comparatively slow as −25 °C and required 72 h for about 90% competion (eq 9). The oxidation of the intermediate dialkylborane was incomplete after stirring at 55 °C for 4 h. However, the difficulty is overcome by the use of excess alkaline hydrogen peroxide, the cosolvent ethanol, and a longer oxidation time. The product alcohol was separated by distillation and purified by crystallization. The absolute configuration and maximum rotation of 2,2,5,5-tetramethyl-3-hexanol is unknown. The enantiomeric purity of the alcohol was determined by applying the chiral shift reagent $Eu(hfc)_3$ to be 92%. A chiral shift reagent study was performed on the racemic alcohol, prior to the study on the optically active sample. The racemic alcohol was readily prepared by hydroboration of *trans*-2,2,5,5-tetramethyl-3-hexene with $BH_3{\cdot}SMe_2$, followed by oxidation.



(9)

92% ee

The hydroboration of *trans*-stilbene was sluggish at −25 °C (^{11}B NMR indicated the reaction to be only about 15% complete in 24 h). Therefore, it was stirred at 0 °C for 48 h to achieve about 75% completion. The low reactivity of *trans*-stilbene toward $IpcBH_2$ can be accounted for both by its high steric requirements and its possession of a double bond conjugated two phenyl groups. The reaction mixture was oxidized by using the reverse addition technique to minimize hydrolysis of the reactive benzyl boron bond. The product on distillation provided isopinocampheol and a residue containing a mixture of unreacted *trans*-stilbene and 1,2-diphenyl-1-ethanol. The product on purification by "flash chromatography", followed by crystallization, was 65% optically pure by comparison with the rotation available from the literature.

The asymmetric hydroboration of unsymmetrical trans olefins with $IpcBH_2$ is equally effective. Thus, *trans*-2-pentene on hydroboration, followed by oxidation, provided a mixture of 3-pentanol (53%) and 2-pentanol (47%). The optical purity of 2-pentanol in the presence of the optically inactive 3-pentanol was determined by comparing its rotation with the maximum rotation. The enantiomeric purity determination is based on the assumption that 3-pentanol will act as an inert solvent and will not have any effect on the magnitude of rotation measured in ethyl ether solvent. The rotation measurement of the mixture

(15) For literature on maximum rotations and absolute configurations of organic compounds, see: (a) Klyne, W.; Buckingham, J. "Atlas of Stereochemistry"; Oxford University Press: New York, 1978. (b) Jacques, J.; Gross, C.; Bourcier, S. In "Fundamentals and Methods of Stereochemistry"; Kagan, H. B., Ed.; Georg Thieme Verlag: Stuttgart, 1977; Vol. 4.

Table III. Asymmetric Hydroboration Results of Representative Trans-Disubstituted Olefins with Monoisopinocampheylborane ($IpcBH_2$)[a]

olefin	product alcohols: alcohol	% yield (isolated)	$[\alpha]^{23}_D$, deg	% ee	config
trans-2-butene	2-butanol	73	+9.8 (neat)	73[b]	*S*
trans-3-hexene	3-hexanol	83	+5.3 (neat)	75[c]	*S*
trans-2,2,5,5-tetramethyl-3-hexene	2,2,5,5-tetramethyl-3-hexanol	61	+34.8 (*c* 5, C_2H_5OH)	92[d]	*R*[h]
trans-stilbene	1,2-diphenyl-1-ethanol	69	−36.7 (*c* 1, C_2H_5OH)	65[e]	*R*
trans-2-pentene	2-pentanol (47%), 3-pentanol (53%)	78	+12.95 (*c* 7.39, Et_2O)	70[f]	*S*
trans-4-methyl-2-pentene	4-methyl-2-pentanol (46%), 2-methyl-3-pentanol (54%)	77	+12.5 (neat)	70[d]	*S*
trans-4,4-dimethyl-2-pentene	4,4-dimethyl-2-pentanol (24%), 2,2-dimethyl-3-pentanol (76%)	74	+23.1 (neat)	76[d]	*R*
trans-β-methylstyrene	1-phenyl-1-propanol	72	+20.6 (neat)	76[g]	*R*

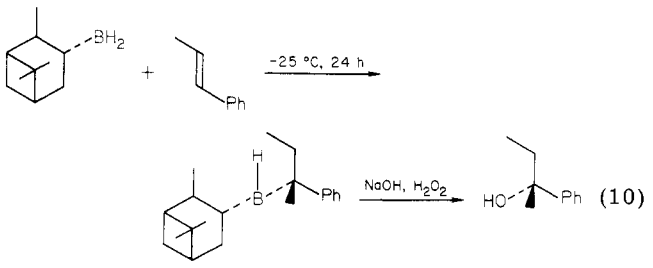
[a] The reactions were carried out on 50-mmol scale in the molar ratio of 1:1. [b] Based on maximum rotation $[\alpha]^{25}_D$ −13.5° (neat): Leroux, P. J.; Lucas, H. J. *J. Am. Chem. Soc.* **1951**, *73*, 41. [c] Based on maximum rotation $[\alpha]^{18}_D$ −7.13° (neat): Kenyon, J.; Poplett, R. *J. Chem. Soc.* **1945**, 273. [d] As determined by 90-MHz NMR with the chiral lanthanide shift reagent tris[[(heptafluoroprop-1-yl)hydroxymethylene]-*d*-camphorato]europium(III) [Eu(hfc)$_3$]. [e] Based on the maximum rotation of $[\alpha]^{18}_D$ +56.1° (*c* 1.0, C_2H_5OH): Berti, G.; Bottari, F.; Ferrarini, P. L.; Macchia, B. *J. Org. Chem.* **1965**, *30*, 4091. [f] Based on maximum rotation $[\alpha]^{20}_D$ +18.5° (*c* 7.39, Et_2O): Levene, P. A.; Mikeska, L. A. *J. Biol. Chem.* **1927**, *75*, 587. [g] Based on maximum rotation $[\alpha]^{17}_D$ −27.35° (neat): Pickard, R. H.; Kenyon, J. *J. Chem. Soc.* **1911**, *99*, 45. [h] The absolute configuration of 2,2,5,5-tetramethyl-3-hexanol has not been established. We predict that (+) isomer is probably *R*.

as the neat liquid, calculating for the 2-pentanol present, also gave a value in close agreement with that measured in ethyl ether.

Similarly, *trans*-4-methyl-2-pentene, on hydroboration–oxidation, provided a mixture of 4-methyl-2-pentanol (46%) and 2-methyl-3-pentanol (54%). The enantiomeric purity of 4-methyl-2-pentanol was determined as 70% by a chiral shift reagent study on the mixture. However, the determination of the enantiomeric purity of 2-methyl-3-pentanol was not successful under those conditions.

Hydroboration of *trans*-4,4-dimethyl-2-pentene, followed by oxidation, provided a mixture of 4,4-dimethyl-2-pentanol (24%) and 2,2-dimethyl-3-pentanol (76%). The regioselectivity observed is rather unusual, and it is not clear at this point why boron attached itself preferentially at the more sterically hindered carbon. The optical purity of the major isomer was determined as 76% by the chiral shift reagent Eu(hfc)$_3$.

The problem of regioselectivity observed in the case of the above unsymmetrical *trans*-alkenes was not encountered in the case of *trans*-β-methylstyrene. The electron-withdrawing phenyl group selectively places the boron atom on the benzylic position. Thus, hydroboration of *trans*-β-methylstyrene with $IpcBH_2$ at −25 °C was complete within 24 h (eq 10). Oxidation of the resulting



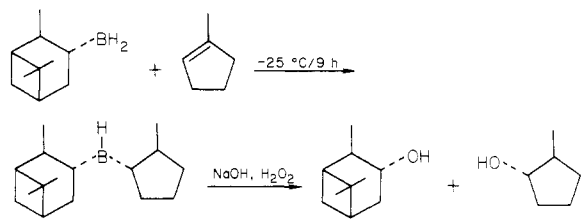
(10)

dialkylborane by using the reverse addition technique provided 1-phenyl-1-propanol without any trace of 1-phenyl-2-propanol. Separation by "flash chromatography" provided pure 1-phenyl-1-propanol. It was 76% enantiomerically pure by rotation data. The results are summarized in Table III.

These results demonstrate for the first time that $IpcBH_2$ can effectively handle both symmetrical and unsymmetrical trans-disubstituted olefins of different structural and steric requirements. The optical activities of the product alcohols are in the range of 65–92% ee. The importance of the steric factor is indicated by the increase in the optical purity of the product in proceeding from *trans*-2-butene to *trans*-3-hexene to *trans*-2,2,5,5-tetramethyl-3-hexene. The enantiomeric purity observed in the case of *trans*-stilbene is lower than that of *trans*-3-hexene, although it is more hindered than the latter. This apparent discrepancy may be caused by some electronic factor associated with *trans*-stilbene.

The absolute configurations of all the product alcohols listed in Table III are known, except for 2,2,5,5-tetramethyl-3-hexanol. Realization of the same absolute configurations in all cases establishes that $IpcBH_2$ must preferentially attack from one enantiotopic face of the *trans*-alkene. In fact, among the several alcohols obtained by using $IpcBH_2$, not a single exception was observed during the entire study. The remarkable consistency of $IpcBH_2$ in providing alcohols of the same absolute configuration can be useful in making configurational assignments and structural correlations. Thus we have assigned the *R* configuration to the (+) isomer of 2,2,5,5-tetramethyl-3-hexanol. Some alcohols listed in Table III have the *R* notation because of the Cahn–Ingold–Prelog priority assignment but actually possess the same sense of absolute configuration.

Hydroboration of Representative Aliphatic Trisubstituted Olefins with $IpcBH_2$. In contrast to Ipc_2BH, monoisopinocampheylborane reacts smoothly with trisubstituted olefins without any significant displacement of α-pinene. The hydroboration of 2-methyl-2-butene and 2-methyl-2-pentene, followed by oxidation, provided the corresponding alcohols in 53% and 58% ee. Similarly, 1-methylcyclopentene on hydroboration with optically pure $IpcBH_2$, followed by oxidation, provided *trans*-2-methylcyclopentanol in 66% ee (eq 11). (In an earlier study, the



(11)

Table IV. Asymmetric Hydroboration Results of Representative Aliphatic Trisubstituted Olefins with Monoisopinocampheylborane ($IpcBH_2$)[a]

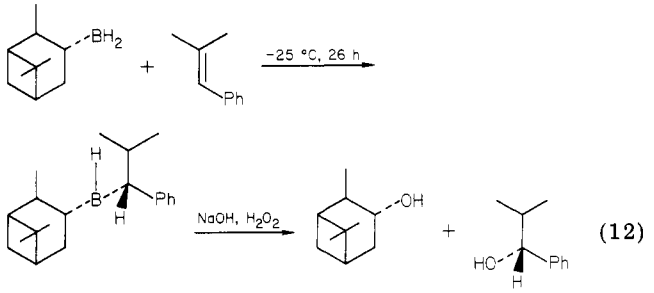
olefin	product alcohols: alcohol	% yield (isolated)	$[\alpha]^{23}_D$, deg	% ee	config
2-methyl-2-butene	3-methyl-2-butanol	75	+2.65 (neat)	53[b]	*S*
2-methyl-2-pentene	2-methyl-3-pentanol	78	−8.63 (neat)	58[c]	*S*
1-methylcyclopentene	*trans*-2-methylcyclopentanol	82	+29.0 (*c* 1, CH_3OH)	66[d]	1*S*,2*S*
1-ethylcyclopentene	*trans*-2-ethylcyclopentanol	78	+29.9 (*c* 5.8, C_2H_5OH)	60[e]	1*S*,2*S*[g]
1-methylcyclohexene	*trans*-2-methylcyclohexanol	85	+31.2 (neat)	72[f]	1*S*,2*S*

[a] The reactions were carried out on 50-mmol scale in the molar ratio of 1:1. The percent enantiomeric excess is based on the maximum rotations (see footnotes *b*–*d*). [b] Sanderson, W. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1966**, *88*, 4185; α^{27}_D +8.12° (*l* = 2, neat) for 3-methyl-2-butanol. [c] Pickard, R. H.; Kenyon, J. *J. Chem. Soc.* **1912**, *101*, 620; $\alpha^{21.4}_D$ +12.4° (*l* = 1, neat) for 2-methyl-3-pentanol. [d] Partridge, J. J.; Chadha, N. K.; Uskoković, M. R. *J. Am. Chem. Soc.* **1973**, *95*, 532; α^{25}_D +43.9° (*c* 1.00, CH_3OH) for *trans*-2-methylcyclopentanol. [e] Determined by 90-MHz NMR with the chiral lanthanide shift reagent Eu(hfc)$_3$. [f] The result taken from earlier study.[9] [g] The absolute configuration of *trans*-2-ethylcyclopentanol has not been established. We predict that the (+) isomer is probably 1*S*,2*S*.

optical purity of *trans*-2-methylcyclopentanol was reported to be 55.4% on using $IpcBH_2$ of 94% ee.) Other examples are listed in Table IV. These results demonstrate that $IpcBH_2$ is indeed a very effective chiral hydroborating agent for aliphatic trisubstituted alkenes. The enantiomeric purities of the product alcohols increased with an increase in the steric requirements of the olefins.

Hydroboration of Representative Phenyl-Substituted Trisubstituted Olefins with $IpcBH_2$. The results obtained in the case of trans-disubstituted and aliphatic trisubstituted olefins clearly indicate that the enantiomeric purities of the product alcohols depend upon the steric requirements of the olefins. On the basis of these observations, it was surmised that it may be possible to match the steric requirements of the chiral hydroborating agent with that of the olefin so as to provide optimum steric fit and thus optimum asymmetric induction. The steric requirements of the present chiral hydroborating agent are constant. However, variations can be made in the steric requirements of the olefins. The results with aliphatic trisubstituted olefins (Table IV) also indicate the possibility for increasing the enantiomeric purities of the alcohols by increasing the steric hindrance and steric fit of the olefins with reagent. Replacement of one of the alkyl groups by a phenyl group provided phenyl-substituted trisubstituted olefins with enhanced steric requirements.

The hydroboration of β,β-dimethylstyrene with $IpcBH_2$, followed by oxidation, provided 1-phenyl-2-methyl-1-propanol with 72% ee (eq 12).

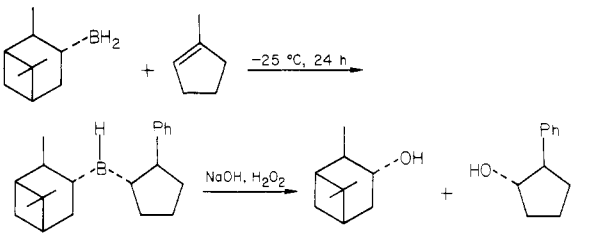


(12)

The hydroboration of (*E*)- and (*Z*)-2-phenyl-2-butenes, followed by oxidation, yielded *threo*- and *erythro*-3-phenyl-2-butanols in 81% and 82% ee, respectively. Similarly, (*E*)- and (*Z*)-3-phenyl-2-pentenes were hydroborated with the reagent to yield, following oxidation, *threo*- and *erythro*-3-phenyl-2-pentanols in 85.5% and 85% ee, respectively. Apparently, both *E*- and *Z*-trisubstituted olefins are hydroborated with an equally high degree of asymmetric induction.

It should be noted that *E* olefins on hydroboration–oxidation provide threo alcohols, whereas the diastereoisomeric erythro alcohols are obtained by the hydroboration–oxidation of the *Z* olefins. Therefore, in cases where two chiral centers are created by hydroboration and two geometric isomers of the olefin are available, it is possible to prepare all four isomers by using $IpcBH_2$ derived from the appropriate antipode of α-pinene and the appropriate geometric isomer of the olefin.

The hydroboration of 1-phenylcyclopentene proved most satisfactory. Thus, 1-phenylcyclopentene on hydroboration with the reagent, followed by oxidation, furnished *trans*-2-phenylcyclopentanol in 100% ee (eq 13). Apparently



(13)

the steric requirement of 1-phenylcyclopentene are optimum and provide a nearly perfect steric match for $IpcBH_2$. The hydroboration of 1-phenylcyclohexene with the reagent was much slower. Even at 0 °C, the reaction required about 7 days to achieve 80% completion. Subsequent oxidation furnished *trans*-2-phenylcyclohexanol in 88% ee. The results observed with phenyl-substituted olefins are summarized in Table V.

The enantiomeric purities appear to increase with increasing steric requirements of the olefins. However, the enantiomeric purity decreases in the case of 1-phenylcyclohexene, although it is the most hindered trisubstituted olefin studied. Possibly the steric requirements of 1-phenylcyclohexene are greater than are optimum for this chiral hydroborating agent. Some support for this hypothesis is provided by the very sluggish reaction of the 1-phenylcyclohexene with the $IpcBH_2$.

Conclusion

Monoisopinocampheylborane is evidently an excellent chiral hydroborating agent for trans and trisubstituted olefins. Unfortunately, it is not clear at this time why the results realized with trans olefins are more favorable than those with aliphatic trisubstituted olefins, although the steric requirements of the latter class of the olefins should be greater than those of the former. Nevertheless, $IpcBH_2$ is effective for olefins with a broad range of steric and structural requirements. The product alcohols are obtained in exceptionally high enantiomeric purities. The new asymmetric center at the alcohol position consistently

Table V. Asymmetric Hydroboration Results of Representative Phenyl-Substituted Trisubstituted Olefins with Monoisopinocampheylborane ($IpcBH_2$)[a]

olefin	product alcohols				
	alcohol	% yield (GLC)	$[\alpha]^{23}_D$, deg	% ee	config
β,β-dimethylstyrene	1-phenyl-2-methyl-1-propanol	88	+21.26 (c 2.9, C_2H_5OH)	72[b]	R
(E)-2-phenyl-2-butene	*threo*-3-phenyl-2-butanol	89	+16.2 (c 3.6, C_2H_5OH)	81[b]	2S,3R
(Z)-2-phenyl-2-butene	*erythro*-3-phenyl-2-butanol	91	−0.5 (c 4.9, C_2H_2OH)	82[b]	2S,3S
(E)-3-phenyl-2-pentene	*threo*-3-phenyl-2-pentanol	87	−16.0 (c 3.5, C_2H_5OH)	85.5[b]	2S,3R
(Z)-3-phenyl-2-pentene	*erythro*-3-phenyl-2-pentanol	95	+21.0 (c 4, C_2H_5OH)	85[b]	2S,3S
1-phenylcyclopentene	*trans*-2-phenylcyclopentanol	92	+71.1 (c 11.9, C_2H_5OH)	100[b]	1S,2R
1-phenylcyclohexene	*trans*-2-phenylcyclohexanol	79	+56.0 (c 0.17, C_6H_6)	88[c]	1S,2R

[a] The reactions were carried out on 50-mmol scale in the molar ratio of 1:1. [b] As determined by 90-MHz NMR with the chiral lanthanide shift reagent tris[[(heptafluoroprop-1-yl)hydroxymethylene]-*d*-camphorato]europium(III) [Eu(hfc)$_3$]. [c] Based on a maximum rotation of $[\alpha]_D$ +63.7° (c 0.17, C_6H_6): Berti, G.; Macchia, B.; Macchia, F.; Monti, L. *J. Chem. Soc. C* **1971**, 3371.

contains the same sense of absolute configuration, even though the notation may be different in a few cases because of the Cahn–Ingold–Prelog priority assignments. No exception to this generalization has been encountered thus far.

It is interesting to note that $IpcBH_2$ is a complementary reagent to Ipc_2BH in two respects. (1) Ipc_2BH is an excellent chiral hydroborating agent for cis olefins where $IpcBH_2$ fails to give good asymmetric induction. On the other hand, $IpcBH_2$ gives excellent results with trans and trisubstituted olefins where Ipc_2BH fails. (2) Both of the reagents derived from the same enantiomer of α-pinene provide alcohols of opposite configuration in the case of cis olefins. It is not clear at this time why there is a reversal of configuration, even though the same enantiomer of α-pinene is used to prepare these reagents.

The present result suggests the possibility of developing a family of asymmetric hydroborating agents of varying steric requirements. It would then be possible to select the hydroborating agent that would provide a highly favorable fit with a given olefinic structure. At the present time three of the four major classes of olefins are effectively handled by Ipc_2BH (cis disubstituted) and $IpcBH_2$ (trans disubstituted, trisubstituted). Only the less sterically demanding group, the 2-methyl-1-alkenes, do not yield optically active alcohols in desirable optical purities.

Experimental Section

The reaction flasks and other glass equipment were dried in an oven (140 °C, 12–18 h) and assembled in a stream of dry nitrogen gas. Special experimental techniques used in handling air-sensitive materials are described in detail elsewhere.[1b]

Materials. (+)-α-Pinene ($[\alpha]^{23}_D$ + 48.7° (neat), 95% ee) was received as a gift from Dr. E. Klein of the Dragoco Co., Holzminden, West Germany. It was used after being distilled from a small excess of lithium aluminum hydride ($LiAlH_4$). Anhydrous ethyl ether was available from Mallinckrodt, Inc., and used directly. *N,N,N',N'*-Tetramethyldiamine (TMED) was distilled over excess calcium hydride. Borane–methyl sulfide was purchased from Aldrich Chemical Co. Tetrahydrofuran (THF) was distilled from a small excess of $LiAlH_4$. The alkenes used for this study were commercial products of the highest purity available and were used directly.

Spectra. ^{11}B NMR spectra were recorded by using a Varian FT-80A instrument. The chemical shifts are in δ relative to BF_3·OEt_2. ^1H NMR (90 MHz) spectra were recorded on a Perkin-Elmer R-32 instrument.

GLC analyses were carried out with a Hewlett-Packard 5750 chromatograph using (a) 6 ft × 0.25 in. column packed with 10% Carbowax 20M on Chromosorb W (60–80 mesh) or (b) a 6 ft × 0.25 in. column packed with 10% SE-30 on Chromosorb W (60–80 mesh). For preparative GLC either (c) a 6 ft × 0.5 in. column packed with 10% Carbowax 20M on Chromosorb W (60–80 mesh) or (d) a 6 ft × 0.5 in. column packed with 20% SE-30 on Chromosorb W (60–80 mesh) was used. GLC analyses of 3- and 2-pentanols, 4-methyl-2-pentanol, 2-methyl-3-pentanol, 4,4-dimethyl-2-pentanol, and 2,2-dimethyl-3-pentanol were carried out on (e) a 50-m capillary column packed with 10% Carbowax 20M by using a Hewlett-Packard 5730A chromatograph.

Preparation of the Bis Adduct of Monoisopinocampheylborane with TMED ($2IpcBH_2$·TMED). A dry, 1000-mL flask equipped with a septum inlet, magnetic stirring bar, and a reflux condenser leading to a mercury bubbler was flushed with dry nitrogen and maintained under a static pressure of nitrogen throughout the preparation. The flask was charged with 51.7 mL (0.5 mol) of neat borane–methyl sulfide and 330 mL of ethyl ether. While the solution was stirred at room temperature, 184 mL (1.15 mol) of α-pinene ($[\alpha]^{23}_D$ +48.7° (neat), 95% ee) was added dropwise at such a rate that the reaction mixture refluxed gently. It was then refluxed for an additional 0.5 h, cooled to room temperature, and treated with 37.7 mL (0.25 mol) of TMED dropwise at such a rate that the reaction mixture was held under gentle reflux. It was further refluxed for 0.5 h. Seedings of $2IpcBH_2$·TMED were introduced into the flask by means of taking out an aliquot of solution from the reaction mixture with a hypodermic syringe and pushing it back into the solution two or three times. The reaction mixture was then allowed to cool at room temperature while $2IpcBH_2$·TMED crystallized out of the solution. The flask was stored at 0 °C for ~18 h to ensure complete crystallization. The supernatant liquid was removed with the help of a double-ended needle, and the crystals of $2IpcBH_2$·TMED were washed (3 × 140 mL) with portions of cold pentane. The solid was dried under vacuum (1 h at 15 mm and 10 h at 1 mm) to yield 76.9 g (74%) of $2IpcBH_2$·TMED: mp 140.5–141.5 °C; $[\alpha]^{23}_D$ +69.03° (c 9.33, THF); ^{11}B NMR (THF, relative to BF_3·OEt_2) 1.80 (br s). The solid was dissolved in 220 mL of THF and transferred to a graduated cylinder to make a total volume of 308 mL. Thus, a 0.6 M solution of $2IpcBH_2$·TMED in THF was made and conveniently stored at room temperature.

Generation of Monoisopinocampheylborane from $2IpcBH_2$·TMED. A 250-mL flask with a magnetic stirring bar and septum was charged with 83.3 mL (50 mmol) of the THF solution of $2IpcBH_2$·TMED. While the solution was stirred at room temperature, 12.3 mL (100 mmol) of BF_3·OEt_2 was added dropwise over 3–5 min, and the reaction mixture was allowed to stir at room temperature for 2 h. Meanwhile, a 250-mL flask with a septum inlet, a magnetic stirring bar, and a filtration chamber was assembled under dry nitrogen and cooled to 0 °C in an ice bath. The resulting slurry from the reaction falsk was transferred under nitrogen to the filtration chamber. The solid $2BF_3$·TMED was washed with portions (3 × 13 mL) of dry, ice-cold THF. The filtrate was analyzed for $IpcBH_2$ by hydrolysis with 1:1:1 glycerol, water, and THF as the hydrolyzing mixture and found to be 0.8213 M; 104.7 mL (86 mmol), 86% yield. The standard solution of $IpcBH_2$ in THF was used immediately for hydroboration.

Reaction of Olefins with Monoisopinocampheylborane in the Molar Ratio of 1:1. Structure of Reaction Intermediates. The following procedure is representative. In a dry 50-mL flask equipped with a septum inlet, magnetic stirring bar, and

a connecting tube leading to a mercury bubbler was placed 6.1 mL (5 mmol) of a 0.8213 M solution of $IpcBH_2$ in THF. It was cooled and maintained at −25 °C by using a commercially available low-temperature bath (Neslab, Inc.). To the flask was added 0.732 g (5 mmol) of (*E*)-3-phenyl-2-pentene dropwise. Stirring was continued for 48 h at −25 °C. The internal standard, 0.42 g (2.46 mmol) of *n*-dodecane, was added, followed by methanolysis of the reaction mixture. The ^{11}B NMR of the methanolyzed product indicated a mixture of methoxydialkylborane (~78%), dimethoxymonoalkylborane (~20%), and trimethoxyborane (~2%). A 3-mL aliquot was taken in a 50-mL flask and THF removed under aspirator vacuum [25 °C (15 mm), 2 h]. The ^1H NMR of the THF-free residue in acetone-d_6 provided the amounts of methoxydialkylborane (83%) and dimethoxyalkylborane (15%). The remaining reaction mixture was oxidized with 1.5 mL 3 M sodium hydroxide, followed by 1.5 mL of 30% hydrogen peroxide. The reaction mixture was maintained at 55 °C for 1 h to ensure completion of oxidation. The queous layer was saturated with potassium carbonate and the organic layer was analyzed by GLC on the column a. The results of our study are summarized in Table I.

(*S*)-(−)-2-Methyl-1-butanol. In a 250-mL flask equipped with septum inlet, magnetic stirring bar, and a connecting tube leading to a mercury bubbler was placed 60.1 mL (50 mmol) of a 0.831 M solution of $IpcBH_2$ in THF, and this was cooled to −25 °C. To the reaction flask was added with stirring 5.4 mL (50 mmol) of 2-methyl-1-butene over a period of 5 min. The reaction mixture was allowed to stir at −25 °C for 4 h. It was then treated with 4 mL (100 mmol) of methanol dropwise at −25 °C (H_2 evolution!) and slowly warmed to room temperature. The organoboranes were then oxidized by successive addition of 18.3 mL of 3 M sodium hydroxide and 18 mL of 30% hydrogen peroxide. The contents were maintained at 55 °C for 1 h to ensure completion of oxidation. The two layers were separated after cooling, and the aqueous layer was extracted with portions (3 × 50 mL) of ethyl ether. The combined organic layer was washed with 30 mL of water and 30 mL of brine and dried over anhydrous magnesium sulfate. The organic extract on fractional distillation with a Widmer column provided 3.32 g of 2-methyl-1-butanol: bp 129–130 °C (748 mm); 76% yield (>96% GLC pure). It was purified on preparative GLC by using column d, to yield GLC pure material: $[\alpha]^{23}_D$ −0.088° (neat), 1.5% ee.

(*S*)-(+)-2-Butanol from *cis*-2-Butene. In a 250-mL flask equipped with septum inlet, magnetic stirring bar, and a connecting tube leading to a mercury bubbler was placed 60.1 mL (50 mmol) of a 0.831 M solution of $IpcBH_2$ in THF, and this was cooled to −25 °C. Meanwhile, 4.5 mL (50 mmol) of *cis*-2-butene was condensed in a graduated cylinder cooled in a dry ice–acetone bath and added slowly to the reaction flask with a double-ended needle. The reaction mixture was stirred at −25 °C for 4 h, followed by addition of 4 mL (100 mmol) of methanol. The organoboranes were oxidized and worked up as described in the 2-methyl-1-butanol experiment to provide 2.47 g of 2-butanol; bp 98–99 °C (745 mm); 67% yield (>95% GLC pure). The alcohol was further purified by preparative GLC using column d to yield GLC pure material: $[\alpha]^{23}_D$ +3.3° (neat), 24% ee.

(*S*)-(+)-2-Butanol from *trans*-2-Butene. In a 250-mL flask equipped with a septum inlet, a magnetic stirring bar, and a connecting tube leading to a mercury bubbler was placed 60.1 mL (50 mmol) of a 0.831 M solution of $IpcBH_2$ in THF, and this was cooled to −25 °C. Meanwhile, 4.65 mL (50 mmol) of *trans*-2-butene was condensed in a graduated cylinder, cooled in a dry ice–acetone bath, and added slowly to the reaction flask with a double-ended needle. A white precipitate of the dialkylborane separated within 0.5 h of stirring at −25 °C. After being stirred for 9 h at −25 °C, the reaction mixture was methanolyzed, oxidized, and worked up as described in the above experiment to furnish 2.7 g of 2-butanol: bp 98–99 °C (745 mm); 73% yield (>95% GLC pure). It was purified on preparative GLC by using column d to yield GLC pure material: $[\alpha]^{23}_D$ +9.8 (neat), 73% ee.

(*S*)-(+)-3-Methyl-2-butanol. In a 250-mL flask equipped with septum inlet, magnetic stirring bar, and a connecting tube leading to a mercury bubbler was placed 61.9 mL (50 mmol) of 0.8075 M of $IpcBH_2$ in THF and cooled to −25 °C. To the reaction flask was added 5.3 mL (50 mmol) of 2-methyl-2-butene with stirring. After being stirred for 9 h at −25 °C, the reaction mixture was methanolyzed, oxidized, and worked up as described in the 2-methyl-1-butanol experiment to furnish 3.3 g of 3-methyl-2-butanol: bp 110–113 °C (748 mm); 75% yield (>95% GLC pure). It was purified by using column d to provide a GLC pure sample: $[\alpha]^{23}_D$ +2.65° (neat), 53% ee.

(*S*)-(+)-3-Hexanol. With the usual experimental setup, 6.2 mL (50 mmole of *trans*-3-hexene was added slowly to 64 mL (50 mmol) of a 0.7814 M solution of $IpcBH_2$ in THF cooled at −25 °C. The dialkylborane precipitated out after 0.5 h of stirring at −25 °C. The reaction mixture was allowed to stir for 9 h at the same temperature. The reaction mixture on methanolysis, oxidation, and workup, as described in the 2-methyl-1-butanol experiment, provided 4.25 g of 3-hexanol: bp 131–133 °C (748 mm); 83% yield (>98% GLC pure). It was purified by using column c to provide GLC pure material: $[\alpha]_D$ +5.3° (neat), 75% ee.

(*R*)-(+)-2,2,5,5-Tetramethyl-3-hexanol. With the usual experimental setup, 9.8 mL (50 mmol) of *trans*-2,2,5,5-tetramethyl-3-hexene was added dropwise to 60.1 mL (50 mmol) of 0.831 M $IpcBH_2$ in THF cooled to −25 °C. The reaction mixture was allowed to stir at −25 °C for 3 days, followed by treatment with 4.0 mL (100 mmol) of methanol. The oxidation of the methanolyzed product with 33 mL of 3 M NaOH and 37.5 mL of 30% H_2O_2 in the presence of 20 mL of ethanol was complete after the mixture was stirred at 55 °C for 18 h. The residue obtained after the usual workup, followed by distillation, furnished 4.82 g of 2,2,5,5-tetramethyl-3-hexanol: bp 86–88 °C (15 mm); 61% yield (>95% GLC pure). It was crystallized from pentane to provide a GLC-pure sample: mp 53–54 °C; $[\alpha]^{23}_D$ +34.8° (*c* 5, C_2H_5OH). The alcohol was found to be 92% enantiomerically pure by using the chiral shift reagent $Eu(hfc)_3$.

Determination of Enantiomeric Excess by Use of the Chiral Shift Reagent $Eu(hfc)_3$. General Procedure. In a 50-mL flask equipped with septum inlet, magnetic stirring bar, and a connecting tube was placed 2.063 g of $Eu(hfc)_3$ (available from Aldrich), and it was heated under vacuum at 165–170 °C (bath temperature; 1 mm) for 2 h in order to remove any traces of moisture. The reagent was dissolved in CCl_4 and transferred to a 5-mL volumetric flask. About 30 mg of the sample alcohol was dissolved in 0.45 mL of CCl_4 and transferred to an NMR tube. The standard solution of the reagent, 20 mg at a time, was added to the sample and the NMR spectrum recorded. After each addition, the NMR was recorded, and the peaks were examined for any resolution. In most cases the best results were obtained by using about 120–200 mg of the reagent for about 30 mg of the sample. The chiral lanthanide shift reagent NMR examination was performed on the racemic alcohol prior to the optically active sample.

(*R*)-(−)-1,2-Diphenyl-1-ethanol. With the usual experimental setup, 9.01 g (50 mmol) of *trans*-stilbene in 10 mL of THF was added dropwise to 60.1 mL (50 mmole of 0.8213 M $IpcBH_2$ in THF cooled to −25 °C. The reaction mixture was stirred at −25 °C for 24 h and at 0 °C for 48 h. In another 250-mL flask was placed 18.3 mL of 3 M NaOH and 18 mL of 30% H_2O_2. The organoborane was added dropwise with double-ended needle to the alkaline hydrogen peroxide. The contents were stirred at 55 °C for 2 h, followed by the usual workup. The residue obtained after removal of solvent was distilled to provide 7.1 g of isopinocampheol [bp 114–115 °C (6 mm)] and 9.06 g of residue consisting of a mixture of unreacted *trans*-stilbene and the desired alcohol. It was separated by "flash chromatography" into two fractions: fraction I, 10% Et_2O in pentane (10 × 30 mL), 0.651 g of *trans*-stilbene; fraction II, 10% Et_2O in pentane (28 × 30 mL), 2.3 g (69% yield) of 1,2-diphenyl-1-ethanol. The alcohol was crystallized from an ethyl ether–pentane mixture to yield a pure sample: mp 63–64 °C; $[\alpha]^{23}_D$ −36.7° (*c* 1, C_2H_5OH), 65% ee.

(*S*)-(+)-2-Pentanol. With the usual experimental setup, 5.4 mL (50 mmol) of *trans*-2-pentene was added dropwise to 60.0 mL (50 mmol) of 0.8342 M $IpcBH_2$ in THF cooled to −25 °C. After being stirred for 9 h at −25 °C, the reaction mixture was methanolyzed, oxidized, and worked up as described in the 2-methyl-1-butanol experiment to provide 3.44 g of a mixture of 3- and 2-pentanol: bp 116–118 °C (747 mm); 78% yield (>98% GLC pure). The mixture was purified by preparative GLC using column d. It was found to be a 53:47 mixture of 3- and 2-pentanol by GLC using column e. The calculated value of the specific rotations of 2-pentanol from the mixture are $[\alpha]^{23}_D$ +12.95° (*c*

7.39, Et_2O) (70% ee) and $[\alpha]^{23}_D$ +9.46° (neat) (68% ee).

(*S*)-(+)-4-Methyl-2-pentanol. With the usual experimental setup, 6.3 mL (50 mmol) of *trans*-4-methyl-2-pentene was added dropwise to 60.0 mL (50 mmol) of 0.8342 M $IpcBH_2$ in THF cooled to −25 °C. The reaction mixture was stirred for 11 h at −25 °C, methanolyzed, oxidized, and worked up as described in the 2-methyl-1-butanol experiment to provide 3.93 g of a mixture of 4-methyl-2-pentanol and 2-methyl-3-pentanol: bp 130–131 °C (745 mm); 77% yield (>95% GLC pure). The mixture was purified by preparative GLC using column d. It was found to be a 46:54 mixture of 4-methyl-2-pentanol and 3-methyl-2-pentanol, $[\alpha]^{23}_D$ −12.5° (neat). The 90-MHz NMR examination of the mixture in the presence of $Eu(hfc)_3$ indicated that 4-methyl-2-pentanol is 70% optically pure. The percent enantiomeric excess of 3-methyl-2-pentanol could not be determined under those conditions.

(*R*)-(+)-2,2-Dimethyl-3-pentanol. With the usual experimental setup, 7.1 mL (50 mmol) of *trans*-4,4-dimethyl-2-pentene was added dropwise 64.0 mL (50 mmol) of 0.7814 M $IpcBH_2$ in THF. The reaction mixture was stirred for 48 h at −25 °C, methanolyzed, oxidized, and worked up as described in the 2-methyl-1-butanol experiment to give 4.26 g of a mixture of 4,4-dimethyl-2-pentanol and 2,2-dimethyl-3-pentanol: bp 128–129 °C (740 mm); 74% yield (>90% GLC pure). The mixture was purified by preparative GLC using column c: $[\alpha]_D$ +23.1° (neat). There was obtained a 24:76 mixture of 4,4-dimethyl-2-pentanol and 2,2-dimethyl-3-pentanol, as indicated by GLC analysis on column e. The 90-MHz NMR examination of the mixture in the presence of $Eu(hfc)_3$ indicated that the 2,2-dimethyl-3-pentanol is 76% optically pure. However, the percent enantiomeric excess of 4,4-dimethyl-2-pentanol could not be determined under those conditions.

(*R*)-(+)-1-Phenyl-1-propanol. With the usual experimental setup, 6.5 mL (50 mmol) of *trans*-β-methylstyrene was added dropwise to 60.0 mL (50 mmol) of 0.8342 M $IpcBH_2$ in THF cooled to −25 °C. The reaction mixture was stirred for 24 h at −25 °C and was added dropwise to the flask containing a mixture of 18.3 mL of 3 M NaOH and 18 mL of 30% H_2O_2. The reaction mixture was stirred at 55 °C for 2 h to complete oxidation of the organoborane. The usual workup, followed by distillation, provided a 13.8-g mixture of isopinocampheol and 1-phenyl-1-propanol, bp 110–115 °C (6 mm). The mixture (1.35 g) was separated into fractions by "flash chromatography": fraction I, 10% Et_2O in pentane (13 × 30 mL), 0.477 g of 1-phenyl-1-propanol, bp 86 °C (3 mm), 72% yield (100% GLC pure), $[\alpha]^{23}_D$ +20.6° (neat), 76% ee; fraction II, 10% Et_2O in pentane (2 × 250 mL), isopinocampheol with 5% impurity of 1-phenyl-1-propanol.

(*S*)-(−)-2-Methyl-3-pentanol. With the usual experimental setup, 6.1 mL (50 mmol) of 2-methyl-2-pentene was added dropwise to 62.8 mL of 0.7959 M $IpcBH_2$ in THF cooled to −25 °C. After being stirred for 9 h at −25 °C, the reaction mixture was methanolyzed, oxidized, and worked up as described in the 2-methyl-1-butanol experiment. There was obtained 3.97 g of 2-methyl-3-pentanol: bp 126–128 °C (748 mm); 78% yield (>95% GLC pure). It was purified by using column d to furnish a GLC-pure material: $[\alpha]_D$ −8.63 (neat), 58% ee.

(1*S*,2*S*)-(+)-*trans*-2-Methylcyclopentanol. With the usual experimental setup, 5.3 mL (50 mmol) of 1-methylcyclopentene was added dropwise to 64.8 mL of 0.77 M $IpcBH_2$ in THF cooled to −25 °C. The reaction mixture was stirred for 9 h at −25 °C. The methanolysis, oxidation, and workup followed were similar to those described in the 2-methyl-1-butanol experiment. There was obtained 4 g of *trans*-2-methylcyclopentanol: bp 99–100 °C (83 mm); 82% yield (>98% GLC pure). It was purified by using column d to furnish a GLC-pure material: $[\alpha]^{23}_D$ +29.0° (*c* 1, CH_3OH), 66% ee.

(1*S*,2*S*)-(+)-*trans*-2-Ethylcyclopentanol. With the usual experimental setup, 6.0 mL (50 mmol) of 1-ethylcyclopentene was added dropwise to 65.4 mL (50 mmol) of 0.7645 M $IpcBH_2$ in THF cooled to −25 °C, and the reaction mixture was allowed to stir for 9 h at −25 °C. The methanolysis, oxidation, and workup, as described in the 2-methyl-1-butanol experiment gave 4.4 g of *trans*-2-ethylcyclopentanol: bp 104–105 °C (80 mm); 78% yield (>94% GLC pure). The purification with column d provided a GLC-pure material: $[\alpha]^{23}_D$ +29.9° (*c* 5.8, C_2H_5OH), 60% ee, as determined by use of $Eu(hfc)_3$.

(*R*)-(+)-1-Phenyl-2-methyl-1-propanol. With the usual experimental setup, 6.6 g (50 mmol) of β,β-dimethylstyrene was added dropwise to 70.7 mL (50 mmol) of 0.7082 M $IpcBH_2$ in THF and stirred at −25 °C for 26 h. The methanolysis, oxidation, and workup, as described in the 2-methyl-1-butanol experiment, gave a 14.9-g mixture of isopinocampheol and 1-phenyl-2-methyl-1-propanol: bp 90–91 °C (10 mm). The purification with column c gave >90% GLC-pure material. It was recycled on the same column to provide a GLC-pure sample, $[\alpha]^{23}_D$ +21.26° (*c* 2.9, C_2H_5OH). The enantiomeric purity was found to be 72% by use of the chiral shift reagent $Eu(hfc)_3$.

(2*S*,3*R*)-(+)-3-Phenyl-2-butanol. With the usual experimental setup, 6.1 g (50 mmol) of (*E*)-2-phenyl-2-butene was added slowly to 65.4 mL (50 mmol) of 0.7645 M $IpcBH_2$ in THF at −25 °C. After stirring for 48 h at −25 °C, the reaction mixture was methanolyzed, oxidized, and worked up as described in the 2-methyl-1-butanol experiment. There was obtained a 14.4-g mixture of isopinocampheol and *threo*-3-phenyl-2-butanol, bp 83–85 °C (3 mm). Two successive purifications with column c furnished a GLC-pure sample, $[\alpha]^{23}_D$ +16.2° (*c* 3.6, C_2H_5OH). The percent enantiomeric excess was 81% by use of the chiral shift reagent $Eu(hfc)_3$.

(2*S*,3*S*)-(−)-3-Phenyl-2-butanol. With the usual experimental setup, 6.1 g (50 mmol) of (*Z*)-2-phenyl-2-butene was added dropwise to 63.2 mL (50 mmol) of 0.79 M $IpcBH_2$ in THF at −25 °C. The reaction mixture was stirred at −25 °C for 48 h, methanolyzed, oxidized, and worked up in the manner described in the 2-methyl-1-butanol experiment to provide a mixture of isopinocampheol and *erythro*-3-phenyl-2-butanol, bp 84–85 °C (3 mm). Two successive purifications with column c furnished a GLC-pure sample: $[\alpha]^{23}_D$ −0.5° (*c* 4.9, C_2H_5OH), 82% ee [by use of $Eu(hfc)_3$].

(2*S*,3*R*)-(−)-3-Phenyl-2-pentanol. With the usual experimental setup, 8.1 mL (50 mmol) of (*E*)-3-phenyl-2-pentene was added dropwise to 63.9 mL (50 mmol) of 0.782 M $IpcBH_2$ in THF at −25 °C. After the contents were stirred for 48 h at −25 °C, the reaction mixture was methanolyzed, oxidized, and worked up in the usual manner. There was obtained a 15.4-g mixture of isopinocampheol and *threo*-3-phenyl-2-pentanol: bp 90–91 °C (3 mm). Two successive purifications on column d gave GLC-pure material: $[\alpha]^{23}_D$ −16.0° (*c* 3.5, C_2H_5OH), 85.5% ee [by use of $Eu(hfc)_3$].

(2*S*,3*S*)-(+)-3-Phenyl-2-pentanol. With the usual experimental setup, 7.36 g (50 mmol) of (*Z*)-3-phenyl-2-pentene was added dropwise to 63.9 mL (50 mmol) of 0.782 M $IpcBH_2$ in THF at −25 °C. The reaction mixture was allowed to stir at −25 °C for 48 h, methanolyzed, oxidized, and worked up as described in the 2-methyl-1-butanol experiment. There was obtained 14.9 g mixture of isopinocampheol and *erythro*-3-phenyl-2-pentanol: bp 87–88 °C (3 mm). It was purified twice by using column d to provide a GLC-pure sample: $[\alpha]^{23}_D$ +21.0° (*c* 4, C_2H_5OH), 85% ee [by use of $Eu(hfc)_3$].

(1*S*,2*R*)-(+)-*trans*-2-Phenylcyclopentanol. With the usual experimental setup, 7.4 mL (50 mmol) of 1-phenylcyclopentene was added dropwise to 64.0 mL (50 mmol) of 0.7812 M $IpcBH_2$ in THF at −25 °C. The contents, after being stirred for 24 h at −25 °C, were methanolyzed, oxidized, and worked up in the usual manner to provide 5.72 g of *trans*-2-phenylcyclopentanol: bp 129–131 °C (6 mm); 71% yield (>99% GLC pure). It was then purified by preparative GLC with column d to give GLC-pure material: $[\alpha]^{23}_D$ +71.1° (*c* 11.9, C_2H_5OH), 100% ee [by use of $Eu(hfc)_3$].

(1*S*,2*R*)-*trans*-2-Phenylcyclohexanol. With the usual experimental setup, 7.9 g (50 mmol) of 1-phenylcyclohexene was added dropwise to 69.0 mL (50 mmol) of 0.7236 M $IpcBH_2$ in THF at 0 °C. The reaction mixture was stirred at 0 °C for 7 days, methanolyzed, oxidized, and worked up in the usual manner. There was obtained 6.1 g of *trans*-2-phenylcyclohexanol: bp 141–143 °C (3 mm); 70% yield (>97% GLC pure). It was crystallized from pentane to give GLC-pure material: mp 64–65 °C; $[\alpha]^{23}_D$ +56.0° (*c* 0.17, C_6H_6), 88% ee.

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(+)-α-pinene of high rotation.

Registry No. $IpcBH_2$, 64234-27-1; $2IpcBH_2$·TMED, 67826-92-0; $IpcBR_2$ (R = 2-methylbut-1-yl), 83615-68-3; IpcBHR R = 2-methylbut-1-yl), 83632-57-9; IpcBHR (R = *sec*-butyl), 83615-69-4; IpcBHR (R = 2-methylbut-3-yl), 83615-70-7; IpcBHR (R = 2-methylpent-3-yl), 83615-71-8; IpcBHR (R = 2-methylcyclopentyl), 83615-72-9; IpcBHR (R = 2-ethylcyclopentyl), 83615-73-0; IpcBHR (R = 3-phenylpent-2-yl), 83615-74-1; IpcBHR (R = 2-phenylcyclopentyl), 83679-39-4; IpcBHR (R = 2-phenylcyclohexyl), 83615-75-2; boranemethyl sulfide, 13292-87-0; (+)-α-pinene, 7785-70-8; 2-methyl-1-butene, 563-46-2; *trans*-2-butene, 624-64-6; 2-methyl-2-butene, 513-35-9; 2-methyl-2-pentene, 625-27-4; 1-methylcyclopentene, 693-89-0; 1-ethylcyclopentene, 2146-38-5; (*E*)-3-phenyl-2-pentene, 4165-86-0; 1-phenylcyclopentene, 825-54-7; 1-phenylcyclohexene, 771-98-2; (*S*)-(−)-2-methyl-1-butanol, 1565-80-6; (*S*)-(+)-2-butanol, 4221-99-2; (*S*)-(+)-3-methyl-2-butanol, 1517-66-4; *cis*-2-butene, 590-18-1; (*S*)-(+)-3-hexanol, 6210-51-1; *trans*-3-hexene, 13269-52-8; (*R*)-(+)-2,2,5,5-tetramethyl-3-hexanol, 79449-64-2; *trans*-2,2,5,5-tetramethyl-3-hexene, 692-48-8; (*R*)-(−)-1,2-diphenyl-1-ethanol, 41822-67-7; *trans*-stilbene, 103-30-0; (*S*)-(+)-2-pentanol, 26184-62-3; 3-pentanol, 584-02-1; *trans*-2-pentene, 646-04-8; (*S*)-(+)-4-methyl-2-pentanol, 14898-80-7; (*S*)-(−)-2-methyl-3-pentanol, 70492-65-8; *trans*-4-methyl-2-pentene, 674-76-0; 4,4-dimethyl-2-pentanol, 6144-93-0; (*R*)-(+)-2,2-dimethyl-3-pentanol, 38636-36-1; *trans*-4,4-dimethyl-2-pentene, 690-08-4; (*R*)-(+)-1-phenyl-1-propanol, 1565-74-8; *trans*-β-methylstyrene, 873-66-5; (1*S*,2*S*)-(+)-*trans*-2-methylcyclopentanol, 39947-48-3; (1*S*,2*S*)-(+)-*trans*-2-ethylcyclopentanol, 83708-72-9; (1*S*,2*S*)-(+)-*trans*-2-methylcyclohexanol, 15963-37-8; 1-methylcyclohexene, 591-49-1; (*R*)-(+)-1-phenyl-2-methyl-1-propanol, 14898-86-3; (2*S*,3*R*)-(+)-*threo*-3-phenyl-2-butanol, 53319-09-8; (2*S*,3*S*)-(−)-*erythro*-3-phenyl-2-butanol, 74365-65-4; (2*S*,3*R*)-(−)-*threo*-3-phenyl-2-pentanol, 74365-66-5; (2*S*,3*S*)-(+)-*erythro*-3-phenyl-2-pentanol, 74365-67-6; (1*S*,2*R*)-(+)-*trans*-2-phenylcyclopentanol, 38805-89-9; (1*S*,2*R*)-(+)-*trans*-2-phenylcyclohexanol, 34281-92-0; β,β-dimethylstyrene, 768-49-0; (*E*)-2-phenyl-2-butene, 768-00-3; (*Z*)-2-phenyl-2-butene, 767-99-7; (*Z*)-3-phenyl-2-pentene, 4165-78-0; isopinocampheol, 27779-29-9.

1,4-Dimethoxy-1,3-butadiene as a Donor Diene in Diels–Alder Cycloadditions

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The title compound (DMBU) is a useful diene in [4 + 2] cycloadditions. Since DMBU is readily obtained in two steps from 1,4-dihydroxy-2-butyne, it should be regarded as an inexpensive and abundant starting material. Diels–Alder products were obtained from DMBU and the dienophiles, dimethyl acetylenedicarboxylate, ethyl propiolate, benzyne, fumaronitrile, tetracyanoethene, maleic anhydride, 1,2-dibenzoylethene, diethyl azodicarboxylate, and four 1,4-quinones. The aromatization of some of these products was studied. As determined by gas chromatography and ^1H NMR, DMBU is normally obtained as three isomers *Z,Z*/*Z,E*/*E,E* = (60 ± 3):(34 ± 3):(6 ± 2). While the *Z,Z* form is less reactive, the *Z,E* and *E,E* isomers react with tetracyanoethene at rates similar to that of 1-methoxy-1,3-butadiene.

The work reported here began with the notion that 1,4-dimethoxy-1,3-butadiene (DMBU) could be a useful "donor" diene in Diels–Alder reactions. In fact, the *E,E* isomer had already been used in two isolated cases.[1] One of the features of DMBU was its potential reactivity: of 26 dienes tested, the reactivity with tetracyanoethene (TCNE) was calculated to be highest for DMBU, according to frontier molecular orbital (FMO) theory.[1a] On the basis of rate constants at 20 °C, DMBU ranked fifth at 7.9 on a scale of 9.5 for cyclopentadiene to 0.6 for *cis*-1-methylbutadiene.[1a]

Although the reported synthesis of (*E,E*)-DMBU has the important virtue of being stereospecific, it does require six steps.[1b] There is also a synthesis of DMBU based on the pyrolysis of the not very common tetramethoxybutane.[2a] On the other hand, the two-step path from the readily available 1,4-dihydroxy-2-butyne (eq 1) is quite simple.[2b] Therefore, we proceeded to investigate the diene capabilities of DMBU.

$$HOCH_2C{\equiv}CCH_2OH \xrightarrow{Me_2SO_4} MeOCH_2C{\equiv}CCH_2OMe \xrightarrow{base} \underset{\text{DMBU}}{MeOCH{=}CHCH{=}CHOMe} \quad (1)$$

Table I. Products from 1,4-Dimethoxy-2,3-dicarbomethoxy-1,4-cyclohexadiene (3a)

conditions, eq 3[a]	product	yield, %
NaOH–EtOH/H_2O	4c	75
5% Pd/C, xylene	4b	86
Br_2, $CHCl_3$	4b	78
MnO_2, PhH	4b	86
Me_2SO, 120 °C	4b	67
NBS, CCl_4	4a	100

[a] At reflux temperature unless otherwise noted.

Structurally the closest diene for which DMBU might be a replacement is 1,4-diacetoxy-1,3-butadiene, although either alkoxy or acetoxy groups might be favored for special applications. Currently this diacetate is prepared in 41–49% yield in three steps from cyclooctatetraene.[3a] Because of the versatility of Diels–Alder synthesis, there has been a veritable industry in the last few years devoted to variations in the pattern of dienes with oxy and thio substituents, e.g., alkoxy, siloxy, acetoxy, and furans.[3,4]

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