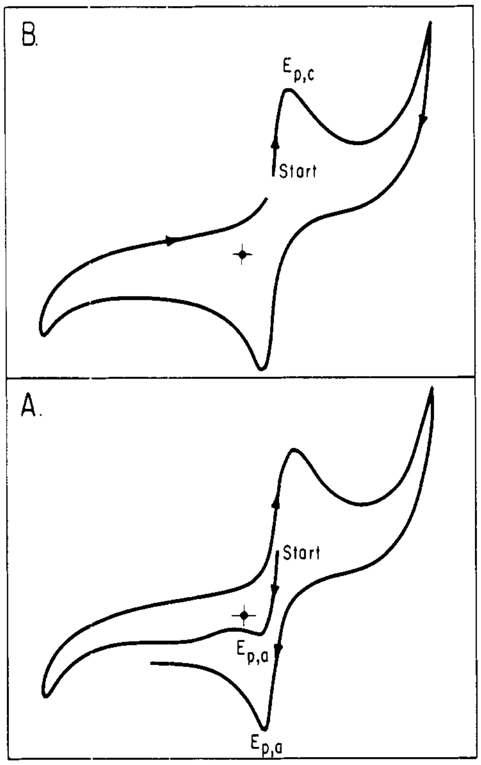

Figure 2. Single-sweep cyclic voltammetry of the 490 quinone performed on the product obtained directly from 3 in an aqueous solution at pH 7.8 (working electrode Au, reference electrode Ag/AgCl): A, anodic sweep; B, cathodic sweep.

confirmation of its structure was provided by the conversion of the natural quinone to 3,4-diacetoxyacetanilide by the following procedure: 15 mL of a 10^{-4} M solution of natural 490 quinone was reduced with an excess of $NaBH_4$, and the solution was acidified with 1 N HCl and taken to dryness under vacuum. The residue was acetylated in Ac_2O and pyridine at 50 °C for 2 h and the solvent removed under vacuum. The crude acetylated product after purification by high-performance LC was identical with authentic 3,4-diacetoxyacetanilide by TLC, high-performance LC, and GC-MS.

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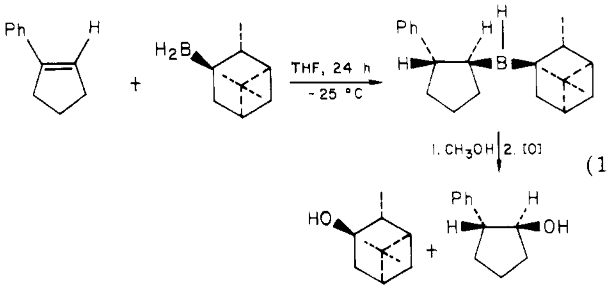
Monoisopinocampheylborane: An Excellent Chiral Hydroborating Agent for Phenyl-Substituted Tertiary Olefins. Synthesis of Alcohols Approaching 100% Enantiomeric Excess

Summary: Monoisopinocampheylborane ($IPCBH_2$), a less hindered chiral hydroborating agent, is highly effective for the hydroboration of phenyl-substituted tertiary olefins, such as 1-phenyl-1-cyclopentene, 1-phenyl-1-cyclohexene, (*E*)- and (*Z*)-2-phenyl-2-butenes, and (*E*)- and (*Z*)-3-phenyl-2-pentenes. Oxidation furnishes alcohols in the range of 81 to 100% ee. The new asymmetric center at the alcohol position is consistently enriched in *S* enantiomer, utilizing reagent prepared from (+)-α-pinene.

Sir: We have recently reported that $IPCBH_2$, a less hindered optically active borane reagent, is highly effective for the asymmetric hydroboration of hindered olefins, such as 1-methyl-1-cyclopentene, 1-methyl-1-cyclohexene, and 2-methyl-2-butene.[1,2] Diisopinocampheylborane (IPC_2BH), an excellent chiral hydroborating agent for cis olefins, hydroborates these hindered olefins only sluggishly, with displacement of α-pinene from the reagent, yielding the corresponding alcohols in only 17–22% ee.[3] In contrast, $IPCBH_2$ hydroborates these olefins cleanly to yield after oxidation the above alcohols in much higher isomeric purities, in the range of 53 to 75% ee. These observations encouraged us to explore the usefulness of $IPCBH_2$ for the hydroboration of other olefins having different steric and structural requirements.

We have now discovered that optically pure $IPCBH_2$, readily available in tetrahydrofuran (THF) by the reaction of TMED·2$IPCBH_2$ with boron trifluoride etherate,[4] hydroborates phenyl-substituted tertiary cyclic or acyclic olefins smoothly to yield after oxidation the corresponding alcohols in exceptionally high optical purities. Thus, hydroboration of 1-phenyl-1-cyclopentene with $IPCBH_2$ in THF at −25 °C requires 24 h for near completion. Oxidation produces *trans*-2-phenylcyclopentanol with an optical purity of 100% ee (eq 1).



(1)

The hydroboration of 1-phenyl-1-cyclohexene with the reagent is much slower. Even at 0 °C, the reaction requires some 7 days to achieve 80% completion. Oxidation furnishes *trans*-2-phenylcyclohexanol in 88% ee.

$IPCBH_2$ is also effective for phenyl-substituted tertiary acyclic olefins. Thus (*E*)- and (*Z*)-2-phenyl-2-butenes are hydroborated with the reagent and yield, following oxidation, optically active (+)-(2*S*,3*R*)- and (−)-(2*S*,3*S*)-3-phenyl-2-butanols in 81% and 82% ee, respectively (eq 2 and 3).

Similarly, the hydroboration of (*E*)- and (*Z*)-3-phenyl-2-pentenes with $IPCBH_2$, followed by oxidation, yields (−)-(2*S*,3*R*)- and (+)-(2*S*,3*S*)-3-phenyl-2-pentanols in 85.5 and 85% ee, respectively.

At this time it is not clear why the results achieved with these phenyl-substituted tertiary olefins are more favorable than those with the corresponding methyl-substituted olefins.

The tosylate derivatives of the optically active 3-phenyl-2-butanols and 3-phenyl-2-pentanols have been

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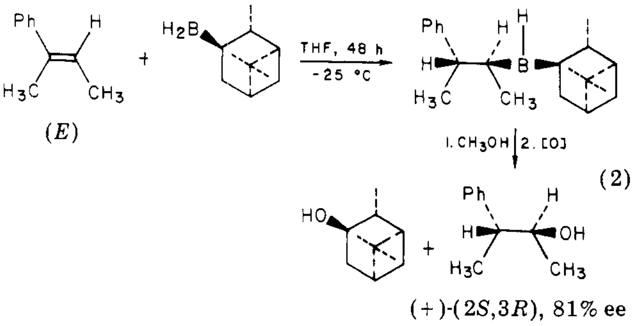
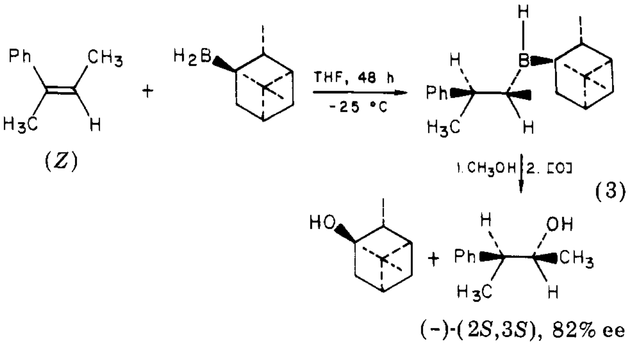
Table I. Asymmetric Hydroboration of Representative Phenyl-Substituted Tertiary Olefins with Monoisopinocampheylborane ($IPCBH_2$)[a] in a 1:1 Ratio[b]

		product alcohols			
olefin	alcohol	yield, % (GC)	$[\alpha]_D$,[c] deg	ee, %	configuration
1-phenylcyclopentene	*trans*-2-phenylcyclopentanol[f]	92	+71.1	100[d]	1*S*,2*R*
1-phenylcyclohexene	*trans*-2-phenylcyclohexanol	79	+56.0 (c 0.17, C_6H_6)	88.0[e]	1*S*,2*R*
(*E*)-2-phenyl-2-butene	(+)-(2*S*,3*R*)-3-phenyl-2-butanol	89	+16.2	81[d]	2*S*,3*R*
(*Z*)-2-phenyl-2-butene	(−)-(2*S*,3*S*)-3-phenyl-2-butanol	91	−0.5	82[d]	2*S*,3*S*
(*E*)-3-phenyl-2-pentene	(−)-(2*S*,3*R*)-3-phenyl-2-pentanol	87	−16.0	85.5[d]	2*S*,3*R*
(*Z*)-3-phenyl-2-pentene	(+)-(2*S*,3*S*)-3-phenyl-2-pentanol[f]	95	+21.0	85[d]	2*S*,3*S*

[a] The reagent is prepared from (+)-α-pinene, $[\alpha]^{23}_D$ +48.5°, 94.8% ee. [b] The reactions were carried out on a 50-mmol scale. [c] $[\alpha]_D$ measured in ethanol (c 5, ethanol). [d] Percent enantiometric excess as determined by 90-MHz NMR using the chiral shift-reagent tris[(3-heptafluoropropylhydroxymethylene)-*d*-camphorato]europium(III) [Eu(hfc)$_3$]. [e] Based on maximum rotation $[\alpha]_D$ +63.7° (c 0.17, C_6H_6): Berti, G.; Macchia, B.; Macchia, F.; Monti, L. *J. Chem. Soc. C* 1971, 3371. [f] NMR studies were made of the effect of the optically active shift reagent on the racemic alcohols indicated. The result revealed no anomaly in the behavior of each isomer.





used in solvolysis reactions to study the role of phenyl participation on the stereochemistry of the products.[5] These optically active alcohols were prepared by the conventional, relatively tedious route involving resolution of the brucine salts of the corresponding phthalate half-esters.[5] However, the present reagent provides a far simpler route to these alcohols in as high or higher enantiomeric excess. The results of our study are summarized in Table I.

It should be noted that in the case of *E* olefins hydroboration takes place preferentially from the top face of the molecules to yield alcohols consistently having *S*,*R* configurations at the two new asymmetric centers, whereas *Z* olefins accept the reagent from the bottom face to yield alcohols having *S*,*S* configurations. In both cases, the configuration of the asymmetric center at the alcohol position is consistently *S*.

The experimental procedure follows. All operations were carried out under nitrogen. TMED·2IPCBH$_2$ was prepared following the reported procedure.[4] A 0.6 M solution of TMED·2IPCBH$_2$ was made in THF. To 53.3 mL (32 mmol) of this solution was added 7.9 mL (64 mmol) of boron trifluoride etherate at 25 °C. The reaction mixture was stirred at 25 °C for 1.25 h. The solution containing free IPCBH$_2$ was then removed from the slurry of TMED·2BF$_3$ by filtration under nitrogen through a filter chamber.[6] The solid TMED·2BF$_3$ was then washed with three 9-mL portions of THF. Thus an 0.8 M solution of IPCBH$_2$ in THF was obtained (confirmed by analysis of an aliquot by hydrolysis). IPCBH$_2$ (62.5 mL, 50 mmol) in THF was cooled to −25 °C. To it was added 1.5 mL of THF (to make the solution 0.7 M in IPCBH$_2$) and then 7.4 mL (50 mmol) of 1-phenyl-1-cyclopentene. The contents of the flask was stirred for 24 h at −25 °C while the dialkylborane precipitated out of the solution. The reaction mixture was brought to 0 °C and 5.0 mL of methanol was added dropwise. Hydrogen, corresponding to 51 mmol, evolved. The solution was treated with 18.4 mL of 3 M sodium hydroxide, followed by 15 mL of 30% aqueous hydrogen peroxide dropwise, maintaining the temperature of the reaction mixture at about 40 °C. After an additional hour at 50 °C, the reaction mixture was cooled and the alcohol products were extracted into ether and dried. Fractional distillation provided 5.72 g of *trans*-2-phenylcyclopentanol, bp 129–131 °C (6 mm), 71% yield. The alcohol was then purified by GLC (SE-30 column); n^{20}_D 1.5455, $[\alpha]^{21}_D$ +71.1° (lit.[7] (maximum rotation) $[\alpha]_D$ +62.1°). Examination of the NMR spectrum of the above alcohol in the presence of chiral shift reagent Eu(hfc)$_3$[8] indicated the alcohol to be 100% enantiomerically pure.

Monoisopinocampheylborane, the first optically active monoalkylborane, is evidently an excellent hydroborating agent for phenyl-substituted tertiary olefins. The reagent is consistent and highly promising for configurational assignments and stereochemical correlations. Furthermore, the ready availability of both (+)- and (−)-α-pinene in high enantiomeric excess provides a convenient route to both enantiomers. Other applications of this reagent in asymmetric organic synthesis are under investigation.

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