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Asymmetric hydroboration of [*E*]- and [*Z*]-2-methoxy-2-butenes. Synthesis of (−)-[2*R*,3*R*]-butane-2,3-diol in >97% ee[†]

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Abstract

Asymmetric hydroboration of [*E*]- and [*Z*]-2-methoxy-2-butene, using (−)-diisopinocampheylborane at −25°C in THF solvent, followed by oxidation using H_2O_2/NaOH, gave (−)-[2*R*,3*R*]- and (+)-[2*R*,3*S*]-3-methoxy-2-butanols in >97 and 90% ee, respectively. (−)-[2*R*,3*R*]-3-Methoxy-2-butanol was converted to (−)-[2*R*,3*R*]-butane-2,3-diol (>97% ee, in an overall yield of 65%). © 2001 Elsevier Science Ltd. All rights reserved.

Asymmetric hydroboration of olefins with diisopinocampheylborane (Ipc_2BH) has been studied extensively. It is known that *cis*-olefins and cyclopentenes react with Ipc_2BH at a reasonable rate to give alcohols of considerate enantiomeric purity.[1] However, the reaction of *trans*-olefins and hindered olefins, such as trialkyl-substituted olefins, with Ipc_2BH is slow and enantioselectivity is known to be poor. For example, the asymmetric hydroboration of *cis*-2-butene using (+)-Ipc_2BH at 0°C was complete in 2 hours and upon oxidation gave (+)-2-butanol in 86–87% enantiomeric excess (ee), whereas reaction of *trans*-2-butene at 0°C took about 24 hours to reach completion and subsequent oxidation produced (−)-2-butanol in only 13% ee.[1] Similarly, asymmetric hydroboration of 1-methylcyclopent-1-ene with Ipc_2BH gives the corresponding 2-methylcyclopentanol in only 22% ee.[1] However, we found that the asymmetric hydroboration of oxy-substituted cyclopentene derivatives **1** with (−)-diisopinocampheylborane ($^{d}Ipc_2BH$), followed by oxidation with H_2O_2/NaOH produces optically active 1,2-cyclopentane diol derivatives **2** in moderate to good (50–85%) ee and good (79–93%) yields.[2]

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Encouraged by our results for the asymmetric hydroboration of oxy-substituted cyclopentenes, we became interested in studying the asymmetric hydroboration of [*E*]-2-methoxy-2-butene to provide the optically active 2,3-butanediol, a valuable chiral auxiliary.[3] To our pleasant surprise, the hydroboration of [*E*]-2-methoxy-2-butene with ^{d}Ipc$_2$BH proceeds very smoothly at −25°C in THF and, after oxidation, (−)-[2*R*,3*R*]-3-methoxybutanol was obtained in 97% ee and in 75% yield. Also, hydroboration of [*Z*]-2-methoxy-2-butene using ^{d}Ipc$_2$BH gave (+)-[2*R*,3*S*]-3-methoxy-2-butanol in 90% ee. Our results are detailed below (Fig. 1).

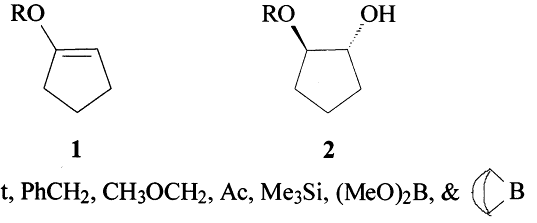
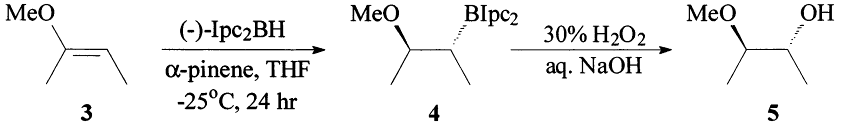


Figure 1.

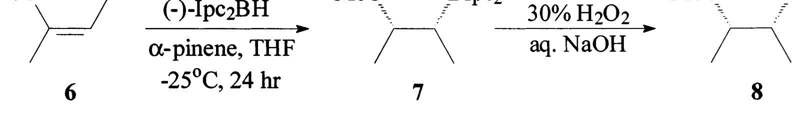
The [*E*]- and [*Z*]-2-methoxy-2-butenes were prepared stereospecifically, starting from *trans*- and *cis*-2-butene, respectively.[4] The asymmetric hydroboration of [*E*]-2-methoxy-2-butene was carried out using ^{d}Ipc$_2$BH at −25°C in THF solvent. The reaction was complete within 24 hours, as indicated by the disappearance of solid ^{d}Ipc$_2$BH and the presence of a single peak in ^{11}B NMR (δ 82 ppm) corresponding to the trialkylborane. Oxidation of the trialkylborane **4** using 30% hydrogen peroxide and aqueous sodium hydroxide gave (−)-[2*R*,3*R*]-3-methoxy-2-butanol[5] **5** in >97% ee[6] and in 72% yield (Scheme 1).[7]



72% isolated yield
>97% ee

Scheme 1.

Similarly, [*Z*]-2-methoxy-2-butene **6**, upon asymmetric hydroboration using ^{d}Ipc$_2$BH, followed by oxidation, gave (+)-[2*R*,3*S*]-3-methoxy-2-butanol[5] **8** of 90% ee[8] in 77% yield (Scheme 2).



77% isolated yield
90% ee

Scheme 2.

The absolute configuration of the products **5** and **6** were determined by comparison of the specific rotation with reported values.[5] The absolute configuration of **5** was also confirmed by its conversion to (−)-[2*R*,3*R*]-2,3-butanediol (see below). The formation of **5** and **6** can be explained based on the lowest energy transition state models,[9] as shown in Fig. 2.

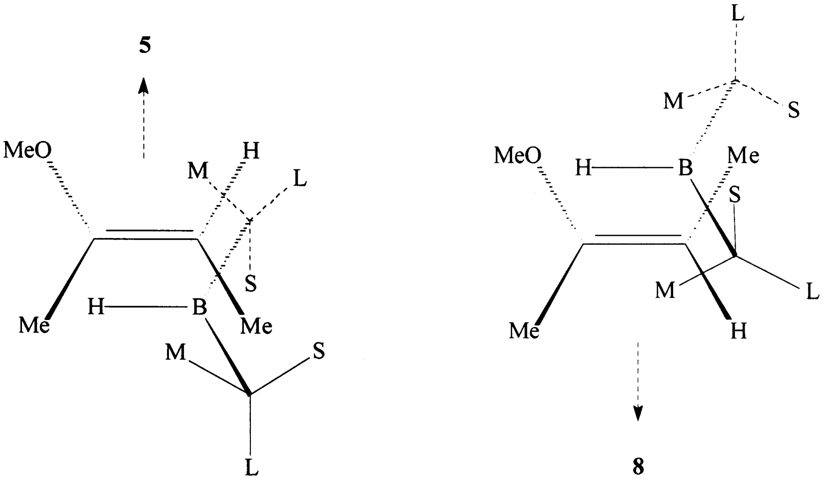
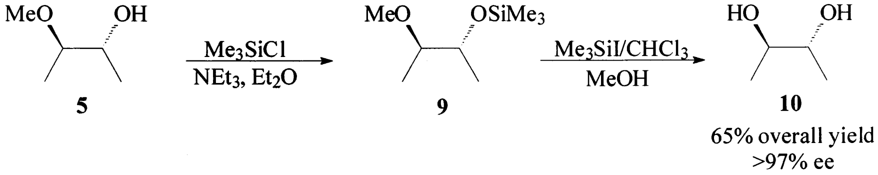


Figure 2. The possible lowest energy transition state models for the formation of compounds **5** and **8**

The [2*R*,3*R*]-3-methoxy-2-butanol was converted[10] to its silyl ether **9** using Me_3SiCl/NEt_3/ether. Reaction of silyl ether **9** with Me_3SiI in $CHCl_3$, followed by treatment with methanol gave (−)-[2*R*,3*R*]-2,3-butanediol[11] (**10**, >97% ee[12]) in 65% overall yield (Scheme 3).



Scheme 3.

In conclusion, although the asymmetric hydroboration of *trans*- and trialkylsubstituted olefins is known to proceed slowly with Ipc_2BH to produce alcohols of very low enantiomeric purity, the hydroboration of [*E*]- and [*Z*]-2-methoxy-2-butenes with $^{d}Ipc_2BH$ proceeded smoothly at −25°C in THF. After oxidation (−)-[2*R*,3*R*]-3-methoxybutanol and (+)-[2*R*,3*S*]-3-methoxy-2-butanol were obtained in very high ee (97 and 90%), respectively. Furthermore, the asymmetric hydroboration of [*E*]-2-methoxy-2-butene using $^{d}Ipc_2BH$, followed by oxidation and then demethylation, provides a useful method for preparing optically active 2,3-butanediol in very high enantiomeric excess and good yield.

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6. The ee of **5** was determined by capillary GC analysis (SPB-5 column at 145°C) of its MTPA ester.
7. The procedure for **5** is typical: To a mixture of ^{d}Ipc$_2$BH[13] (5.72 g, 20 mmol), (+)-α-pinene of 92% ee (0.52 mL, 3 mmol) and THF (11.8 mL) stirred at −25°C was added dropwise (*E*)-2-methoxy-2-butene (1.72 g, 20 mmol) for about 5 min. Stirring was continued at −25°C. After 20 hours ^{11}B NMR showed a single peak at δ 81.96 ppm, corresponding to a trialkylborane. To the reaction mixture kept at −25°C, a 3N aq. NaOH solution (7.0 mL) was added, followed by 30% aq. H_2O_2 (7.0 mL). The mixture was slowly warmed to rt and stirred overnight. After saturating the mixture with K_2CO_3, the organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were dried over Na_2SO_4 and fractionated using a Vigreux column to give pure (2*R*,3*R*)-3-methoxy-2-butanol at 68°C/100 mm of Hg (**5**, 1.5 g, 72%). $[\alpha]_D^{24} = -26.3$ (neat). Lit.[5] −26.2 (neat).
8. The ee of **8** was determined by comparing its optical rotation $[\alpha]_D^{24} = +18.0$ with the reported value[5] ($[\alpha]_D = +20.1$ (neat), for (+)-[2*R*,3*S*]-3-methoxy-2-butanol of 100% enantiomeric excess), as the GC separation of its MTPA ester was unsuccessful.
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10. Preparation of **10**: To a solution of **5** (7.8 g, 75 mmol) in ether (150 mL) was added NEt_3 (12.5 mL, 90 mmol) and Me_3SiCl (11.4 mL, 90 mmol) at rt and the mixture was heated to reflux for 12 h. The precipitated solids were filtered off and the filtrate was fractionated (145°C/750 mm of Hg) to give pure silyl ether **9** (11.0 g, 84% yield). To a solution of **9** (8.8 g, 50 mmol) in $CHCl_3$ (30 mL) was added Me_3SiI (13.5 g, 67.6 mmol). The mixture was heated at 35°C for 12 hours. Methanol (6 mL) was added and stirred at room temp. for 2 h. The volatiles were removed under reduced pressure and the residue was distilled. Pure (−)-[2*R*,3*R*]-butane-2,3-diol **10** was collected at 100°C/30 mm of Hg. Yield 3.5 g (78%). $[\alpha]_D^{24}$ −12.6 (neat).
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