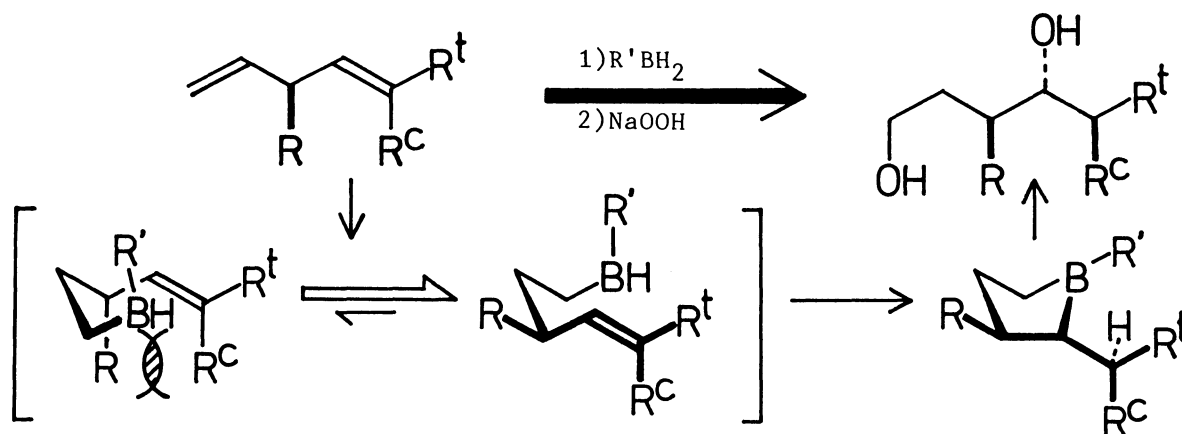


$A^{(1,3)}$ Strain-Controlled Cyclic Hydroboration of 1,4- and 1,5-Dienes

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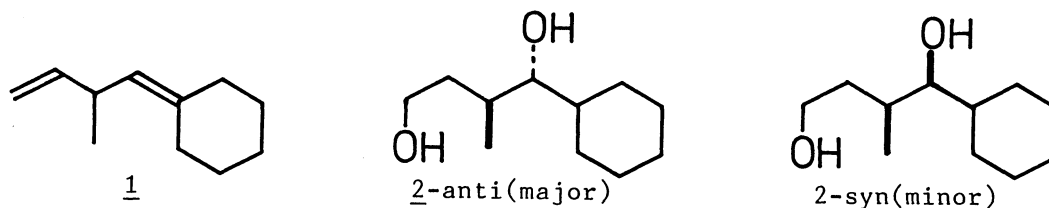
Cyclic hydroboration of 4-cyclohexylidene-3-methyl-1-butene by thexylborane gave 1-cyclohexyl-2-methyl-1,4-butanediol in 96/4 anti/syn ratio in 72% yield. Similarly, 5-cyclohexylidene-4-methyl-1-pentene gave 1-cyclohexyl-2-methyl-1,5-pentanediol in 95/5 anti/syn selectivity in 47% yield by BH_3 . This reaction was applied to the stereoselective preparation of a cyclopentanone.

Stereoselective construction of polyfunctionalized acyclic systems is one of the most important subjects in the synthetic organic chemistry today. Allylic strain,¹⁾ particularly $A^{(1,3)}$ strain is known to be a powerful directing force to lead a reaction by way of the most favorable transition state to give diastereomers in a highly biased ratio.²⁾ Here we report the successful application of the $A^{(1,3)}$ strain to the cyclic hydroboration.³⁻⁵⁾



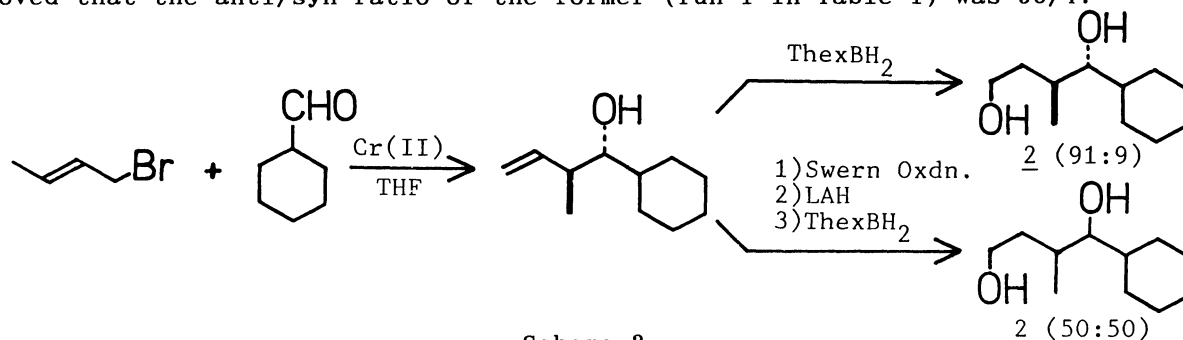
Scheme 1.

We chose 4-cyclohexylidene-3-methyl-1-butene (1)^{6,7)} as the substrate to examine the anti/syn selectivity concerning with the newly formed secondary hydroxyl group and the inherent allylic substituent.



Treatment of 4-cyclohexylidene-3-methyl-1-butene (1) with 1.2 equiv. of thexylborane^{3,8)} at 0.06 mol dm⁻³ diene concentration in THF (-78 °C - r.t.) followed by the usual hydrogen peroxide-sodium hydroxide treatment and purification with flash column chromatography gave a diastereomeric mixture of 1,4-diols 2-anti and 2-syn in 72% yield.

Authentic sample of the anti-rich diol mixture was prepared according to the method of Hiyama and Nozaki; i.e. reaction of a sterically unhindered aldehyde and the *trans*-crotyl bromide in the presence of Cr(II), which is known to produce the anti stereoisomer predominantly⁹⁾ (Scheme 2). A 50/50 anti/syn mixture of the diols was also prepared by way of Swern oxidation and LAH reduction of 3. The 400 MHz ¹H-NMR spectra of our reaction product and the authentic samples proved that the anti/syn ratio of the former (run 1 in Table 1) was 96/4.¹⁰⁾



Scheme 2.

Table 1. Cyclic hydroboration-oxidation of 1,4- and 1,5-dienes 1 and 4^{a)}

Run	Diene	Reagent	Concentration/mol dm ⁻³	Anti/syn ^{b)}	Yield/% ^{c)}
1	<u>1</u>	ThexBH ₂	0.06	96/ 4	72
2	<u>1</u>	BH ₃	0.09	76/24	73
3	<u>1</u>	ThexBH ₂	0.19	78/22	39
4	<u>1</u>	ThexBH ₂	0.01	91/ 9	53
5	<u>4</u>	ThexBH ₂	0.10	97.5/ 2.5	6 ^{d)}
6	<u>4</u>	BH ₃	0.09	95/ 5	47
7 ^{e)}	<u>1</u>	ThexBH ₂	0.10	98/ 2 ^{f)}	49 ^{g)}

a) With 1.2 equiv. borane reagent at -78 °C - r.t. in THF for 40 to 60 min.

b) Determined by 400 MHz ¹H-NMR.

c) Yield of the chromatographically inseparable mixture of anti and syn diols.

d) Obtained together with 40% yield of mono-ol 6 and 28% of recovered diene 4.

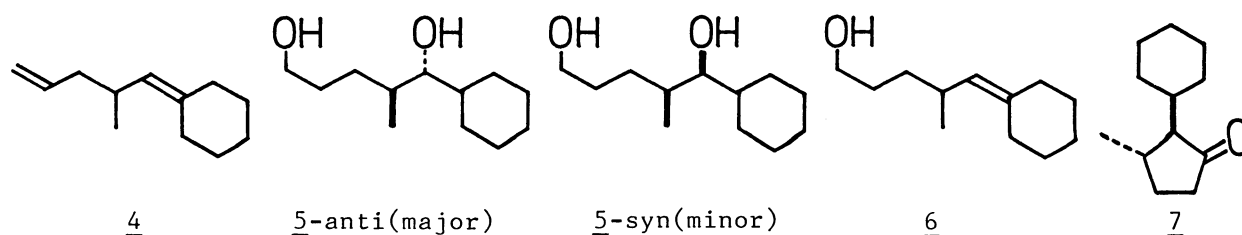
e) Reaction of the cyclopentanone synthesis.

f) Ratio of the diols derived from the cyclopentanone 7.

g) Yield of the cyclopentanone 7.

When BH₃-THF complex was used as the hydroboration reagent, the anti/syn ratio fell down substantially despite the combined yield of the anti and syn diols was comparable (run 2). It is probably because that the *intermolecular* hydroboration of the internal double bond by BH₃ itself competed with the *intramolecular* cyclic hydroboration.

Influence of the concentration of the diene during the reaction was remarkable (runs 1, 3, and 4). The anti/syn ratio of the reaction at 0.19 mol dm⁻³ was merely 78/22 with only 39% yield. At 0.01 mol dm⁻³, however, the diastereoselectivity was not improved.¹¹⁾



When 5-cyclohexylidene-4-methyl-1-pentene (4)¹²⁾ was treated with thexylborane as described above, the major product obtained was shown to be the monohydroborated compound 6 in 40% isolated yield, together with the cyclic-hydroborated diols 5 (6%) and the recovered starting 1,5-diene 4 (28%). Neither the prolonged reaction time at r.t. nor the elevated reaction temperature improved the yield of 5. In spite of the low yield, the anti/syn ratio of the diols thus obtained was 97.5/2.5 (run 5).¹³⁾ That the reaction of 1,4-diene 1 proceeded more smoothly than that of the 1,5-diene 4 would be attributable to the strong tendency of cyclic hydroboration reaction to form a five-membered boracycle when possible.⁴⁾ In order to reduce the steric congestion of the second intramolecular hydroboration of 4, BH_3 -THF complex was therefore employed next (run 6). The yield of 5 raised to 47% together with the recovery of 5% starting diene 4 and no mono-ol 6, and the level of the anti/syn ratio of the diols was kept as high as 95/5.

This reaction was applied to the stereoselective synthesis of a 2,3-trans-disubstituted cyclopentanone (run 7). According to the method reported by Pelter,¹⁵⁾ the boracycle, the reaction intermediate of cyclic hydroboration, was treated with sodium cyanide followed by trifluoroacetic anhydride. After oxidation followed by purification, a ketone 7 was obtained in 49% yield. In order to assess the degree of retention of the stereochemistry during the carbonylation reaction, the ketone was correlated with the diol 5 in two steps: (1) oxidation with mCPBA in CH_2Cl_2 (87%), (2) reduction with LAH in THF (98%). That the anti/syn ratio of the diol 5 thus obtained was 98/2 indicated that the trans/cis ratio of the substituents of the cyclopentanone 7 was 98/2.

In summary, a highly stereoselective cyclic hydroboration controlled by $\text{A}^{(1,3)}$ strain, to obtain acyclic compounds possessing 1,2-anti-2-methyl-1,4-diol system or 1,2-anti-2-methyl-1,5-diol system in greater than 95/5 selectivity, was presented. For the 1,4-diol system from the 1,4-diene, thexylborane showed excellent selectivity, and for the 1,5-diol system from the 1,5-diene, borane was effective. This reaction was shown to be useful to the synthesis of 2,3-trans-disubstituted cyclopentanones and δ -lactones in a stereoselective manner. Work to figure out the scope and limitation of the described methodology and the application to the natural product synthesis in homochiral form is now under way.

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References

- 1) F. Johnson, Chem. Rev., 68, 375(1968).
- 2) Typical recent reports recording high stereoselectivity by the A^(1,3) strain: D. A. Evans, M. M. Morrissey, and R. L. Dow, Tetrahedron Lett., 26, 6005 (1985)(Hydroxyl-directed hydrogenation); M. Hirama, H. Hioki, S. Ito, and C. Kabuto, *ibid.*, 29, 3121(1988)(Intramolecular Michael addition).
- 3) G. Zweifel and H. C. Brown, J. Am. Chem. Soc., 85, 2066(1963); E.-i. Negishi and H. C. Brown, Synthesis, 1974, 77.
- 4) W. C. Still and K. P. Darst, J. Am. Chem. Soc., 102, 7387(1980).
- 5) Although two independent work dealing with the allylic strain-controlled cyclic hydroboration of specific 1,5-dienes, with fair to excellent selectivity, were reported with regard to the synthesis of Prelog-Djerassi lactone, none was found about the 1,4-dienes: D. J. Morgans, Jr., Tetrahedron Lett., 22, 3721(1981); W. C. Still and K. R. Shaw, *ibid.*, 22, 3725(1981).
- 6) Prepared in 4 steps from cyclohexanone.
- 7) Although all the compounds appeared in this communication were racemic, one chiral form was depicted.
- 8) We used thexylborane because it had been successfully employed for the conformation-controlled stereoselective cyclic hydroboration by Still.⁴⁾
- 9) Y. Okude, S. Hirano, T. Hiyama, and H. Nozaki, J. Am. Chem. Soc., 99, 3179 (1977); C. T. Buse and C. H. Heathcock, Tetrahedron Lett., 1978, 1685.
- 10) Integration of the proton signals on the carbon bearing the secondary hydroxyl group in 400 MHz ¹H-NMR was used for the determination of the anti/syn ratio. For the anti isomer, this proton appears at δ 3.12 (t, J=5.9 Hz), while for the syn isomer, it appears at δ 3.21 (dd, J=8.3, 2.9 Hz) (CDCl₃). The authentic anti-rich mixture prepared according to Ref. 9 was shown to be 91/9 (anti/syn), and the anti/syn mixture by way of oxidation-reduction procedure of the secondary alcohol was 50/50.
- 11) The reaction with this concentration was done twice. We have no particular explanation why the anti/syn ratio of this reaction was lower than that of run 1.
- 12) Prepared in 7 steps from cyclohexanone.
- 13) Determination of the stereochemistry of the diols was based on the ¹³C-NMR analysis of the tetrahydropyran derivative obtained by the treatment of 5 with 1.2 equiv. of TsCl in pyridine followed by NaH in THF: While the methyl carbon of the major tetrahydropyran appeared at δ 17.93 (equatorial), that of the minor compound appeared at δ 11.59(axial) (CDCl₃).¹⁴⁾ This implies that the major tetrahydropyran has 2,3-trans diequatorial substituents and was therefore derived from the anti diol, which is the major, allylic strain-controlled product.
- 14) E. L. Eliel, M. Manoharan, K. M. Pietrusiewicz, and K. D. Hargrave, Org. Magn. Reson., 21, 94(1983).
- 15) A. Petler, K. Smith, M. G. Hutchings, and K. Rowe, J. Chem. Soc., Perkin Trans. 1, 1975, 129.

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