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

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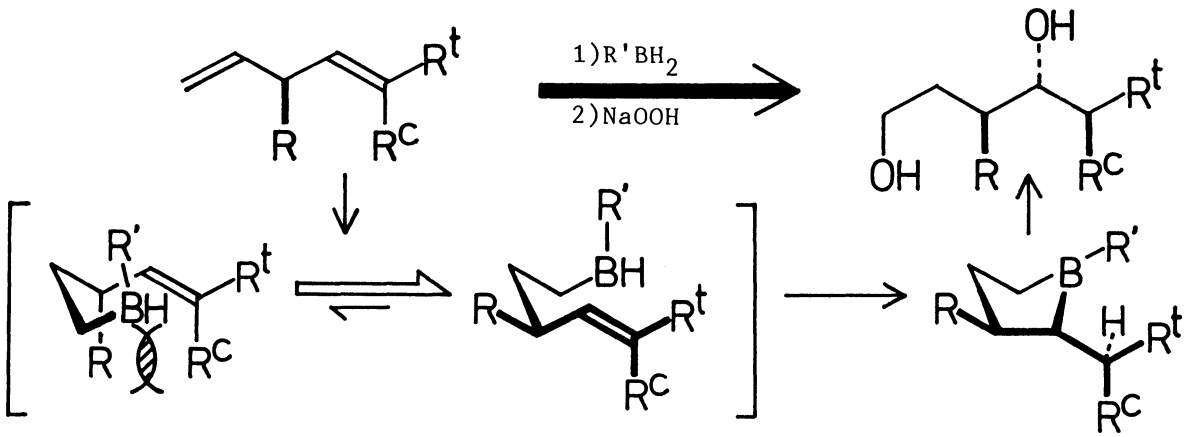
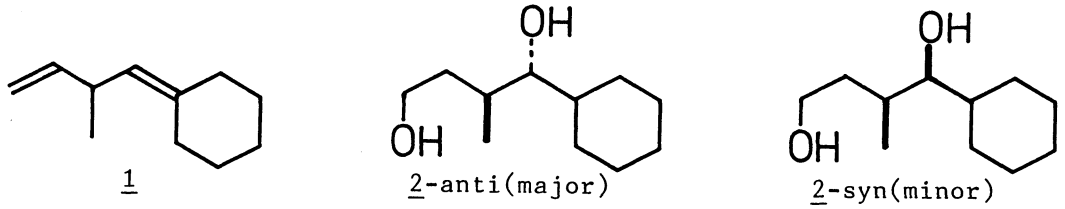
Cyclic hydroboration of 4-cyclohexylidene-3-methyl-1-butene by thexylborane gave 1-cyclohexyl-2-methyl-1,4-butanediol in 96/4 anti/syn ratio in 72% yield. Similarly, 5-cyclohexylidene-4-methyl-1-pentene gave 1-cyclohexyl-2-methyl-1,5-pentanediol in 95/5 anti/syn selectivity in 47% yield by BH_3. This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

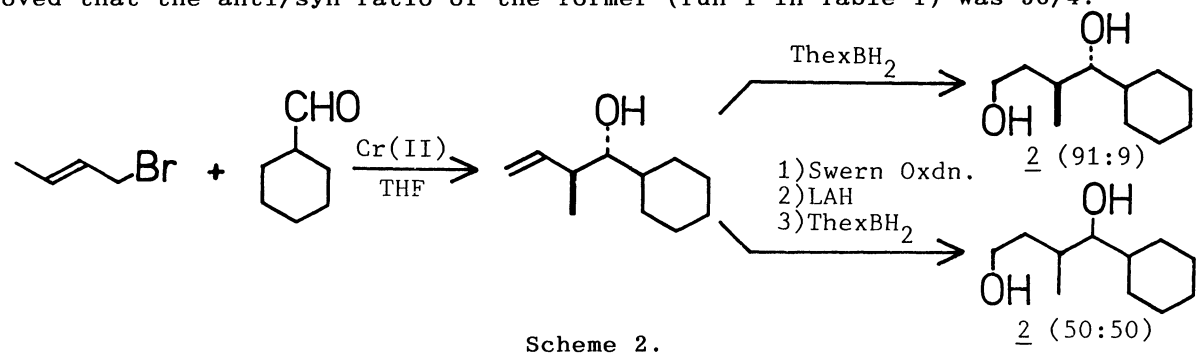
We chose 4-cyclohexylidene-3-methyl-1-butene (1)[6,7] as the substrate to examine the anti/syn selectivity concerning with the newly formed secondary hydroxyl group and the inherent allylic substituent.



1 2-anti(major) 2-syn(minor)

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 predominantly[9] (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 ^{1}H-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.

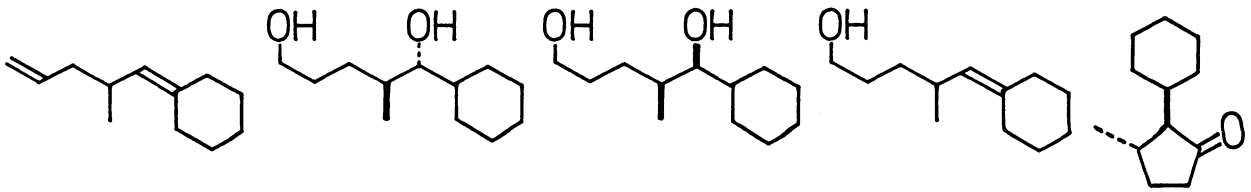
Table 1. Cyclic hydroboration-oxidation of 1,4- and 1,5-dienes 1 and 4[a]

Run	Diene	Reagent	Concentration/mol dm^{-3}	Anti/syn[b]	Yield/%[c]
1	1	$ThexBH_2$	0.06	96/ 4	72
2	1	BH_3	0.09	76/24	73
3	1	$ThexBH_2$	0.19	78/22	39
4	1	$ThexBH_2$	0.01	91/ 9	53
5	4	$ThexBH_2$	0.10	97.5/ 2.5	6[d]
6	4	BH_3	0.09	95/ 5	47
7[e]	1	$ThexBH_2$	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 ^{1}H-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 BH_3-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 BH_3 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]



4 5-anti(major) 5-syn(minor) 6 7

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 hydroboation 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 cyclopentenone 7 was 98/2.

In summary, a highly stereoselective cyclic hydroboration controlled by $A^{(1,3)}$ 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

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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]
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10) Integration of the proton signals on the carbon bearing the secondary hydroxyl group in 400 MHz ^{1}H-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) ($CDCl_3$). 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 ^{13}C-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) ($CDCl_3$).[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.
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