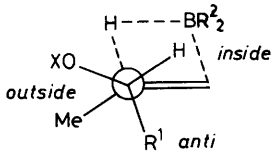
Stereochemical Control of Consecutive Stereogenic Centres by Intramolecular Hydroboration of Dialkenyl Carbinol Derivatives

Toshiro Harada,* Yasuhiro Matsuda, Isao Wada, Junji Uchimura, and Akira Oku*

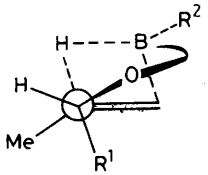
Department of Chemistry, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606, Japan

A simple and efficient method for the stereocontrol of consecutive stereogenic centres was realized by utilizing an intramolecular hydroboration of dialkenyl carbinol derivatives.

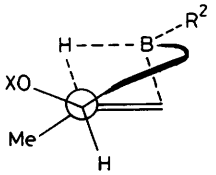
It is well-known that diastereofacial selectivities in hydroboration of alkenes are directed by neighbouring stereogenic centres. Among various examples of this category, hydroborations of secondary allylic alcohol derivatives $R^1CH(OX)C(Me)=CH_2$ are of significant importance for acyclic stereocontrol since an employment of bulky boranes generally provides 1,3-diols with a high *anti* (or *threo*) selectivity with respect to the pre-existing stereogenic centre.[1]



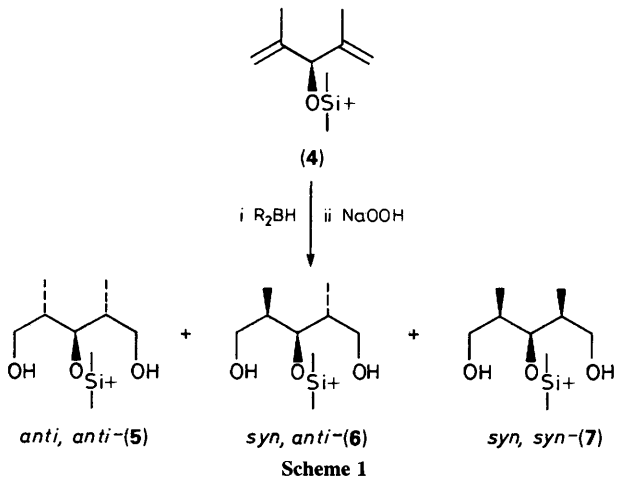
(1)



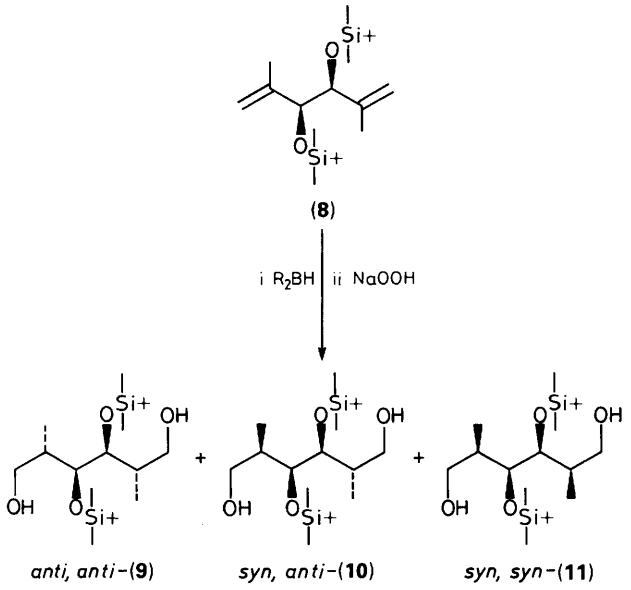
(2)



(3)



Scheme 1



Scheme 2

According to the recent theoretical study of hydroborations by Houk and co-workers,[2] *anti* diols are produced *via* a staggered transition state (**1**) where substituents R^1 and OX take the *anti* and outside positions, respectively. They suggested the importance of a stereoelectronic effect on the *anti* substituent which stabilizes the transition state in the increasing order of OR', H, and alkyl group. In this respect, it is anticipated that, when the intramolecular hydroboration[3,4,5] of allylic alcohol derivatives are performed, *syn*-diols will be selectively produced *via* a transition state (**2**) or (**3**) where OR' or an alkyl group is fixed to the inside position, respectively. Indeed, we recently found that the hydroboration of allyl vinyl ethers proceeds through the transition state of type (**2**) to give *syn*-diols with high stereoselectivities.[6] We wish to report here the intramolecular hydroboration through the transition state of type (**3**) which is applicable to the acyclic stereocontrol of three and four consecutive stereogenic centres.

The double hydroboration of dialkenylcarbinyl silyl ether (**4**) which affords three possible diastereoisomers (**5**), (**6**), and (**7**) were examined using several borane reagents (Scheme 1).† The results are summarized in Table 1.

The hydroboration of (**4**) with 9-borabicyclo[3.3.1]nonane (9-BBN) followed by standard treatment with alkaline hydrogen peroxide gave the *anti,anti*-isomer (**5**) with a high stereoselectivity as anticipated from the double intermolecular reactions (entry 1). In contrast to this, the *syn,anti*-isomer (**6**) was produced with a high selectivity in the reaction with 1,1,2-trimethylpropylborane ($ThexBH_2$) (entry 2). The selectivity observed here can be most reasonably explained by the *anti* selective intermolecular reaction in the first step followed by the intramolecular reaction as the second step which proceeded with high *syn* selectivity as expected from the transition state of type (**3**).

Table 1. Hydroboration of dialkenyl carbinol derivative (**4**).

Entry	Borane(equiv)	Yield/%[a]	(**5**) : (**6**) : (**7**)[b]
1	9-BBN(3.0)	93	13 : 1 : —
2	$ThexBH_2$(3.0)	91	1 : 15 : 1
3	BH_3–THF(2.0)	85	1 : 1.3 : 3.3

[a] Isolated Yield. [b] Ratio was determined by capillary GLC analysis of the tris-TMS (TMS = trimethyl silane) derivatives.

Formation of the *syn,syn*-isomer (**7**) as a major product in the reaction with BH_3–THF (entry 3) is also rationalized by a similar mechanism where the first intermolecular reaction proceeded with a moderate *syn* selectivity. Owing to the lack of experimental data on the stereoselectivity in the reaction of secondary allylic alcohol derivatives with less sterically demanding boranes, we examined the reaction of the t-butyldimethylsilyl ether of 2,4-dimethylpent-1-en-3-ol with BH_3–THF for comparison. In accordance with the above finding, the corresponding *syn*- and *anti*-products were obtained in a ratio of 2.5 : 1 (84% yield).

The synthetic utility of the intramolecular hydroboration was further exemplified in its application to the stereoselective construction of four consecutive stereogenic centres (Scheme 2).‡ The reaction of D,L-(**8**) with 9-BBN (6 equiv.) gave exclusively the *anti,anti*-isomer (**9**) in 90% yield [(**9**) : (**10**) : (**11**) >100 : 1 : 1]. In contrast to this, highly selective formation of the *syn,anti*-isomer (**10**) was observed in the reaction with $ThexBH_2$ (2 equiv.) [62% yield, (**9**) : (**10**) : (**11**) = 1 : 24 : 0].

Still and co-workers have reported that the intramolecular hydroboration of simple symmetric dienes [CH_2=C(Me)-$(CH_2)_n$C(Me)=CH_2; n = 2, 3, or 4] stereoselectively gave the corresponding *meso*-diols.[4] It should be noted that the selectivity observed in the formation of the *syn,anti*-isomers (**6**) and (**10**) was opposite to that in the reaction with simple dienes where the selectivity was controlled, not stereoelectronically but sterically, by the pseudo-equatorial orientation of the alkyl substituent in the cyclic transition state.

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† To a solution of (**4**) in tetrahydrofuran (THF) (1 M) was added a THF solution of borane reagents [9-BBN (0.8 M), $ThexBH_2$ (1 M), BH_3–THF (1 M)] at −85 °C and the resulting mixture was slowly warmed to room temperature during a period of 2—3 h and then stirred overnight. After usual treatment with aq. NaOH–H_2O_2 and aqueous work-up, products were isolated by flash chromatography [(**5**): R_f 0.31, (**6**): R_f 0.27, (**7**): R_f 0.17 (silica gel, 50% ethyl acetate in hexane)]. Structures of (**5**) and (**7**) were determined by converting them to (2*R**, 3*S**, 4*S**)-1-benzyloxy-3,5-dihydroxy-2,4-dimethylpentane (Y. Kishi and H. Nagaoka, *Tetrahedron*, 1981, **37**, 3873) and (2*R**, 3*S**, 4*S**)-1,3,5-trihydroxy-2,4-dimethylpentane 3,5-acetonide (D. V. Patel, F. Van Middlesworth, J. Donaubauer, P. Gannet, and C. J. Sih, *J. Am. Chem. Soc.*, 1986, **108**, 4603), respectively. Stereochemistry of the *syn,anti*-isomer (**6**) was apparent from its ^{1}H NMR spectrum in which two methyl doublets were observable at δ 0.89 and 0.93.

‡ Stereochemistry of the unsymmetrical isomer (**10**) was determined unambiguously from ^{1}H NMR measurements. Determination of the structures of symmetrical isomers (**9**) and (**11**) were done by ^{1}H NMR analyses of their bisacetonide derivatives.