Highly Stereoselective Synthesis of 1,3-Diols utilizing Intramolecular Hydroboration of Allyl Vinyl Ethers

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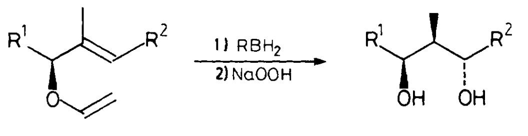
Reaction of secondary allyl vinyl ether with $ThexBH_2$ (Thex = 1,1,2-trimethylpropyl) followed by treatment with alkaline hydrogen peroxide gave the corresponding 1,3-diol with high *syn* selectivity (>16 : 1) with respect to the pre-existing stereogenic centre and the adjacent one.

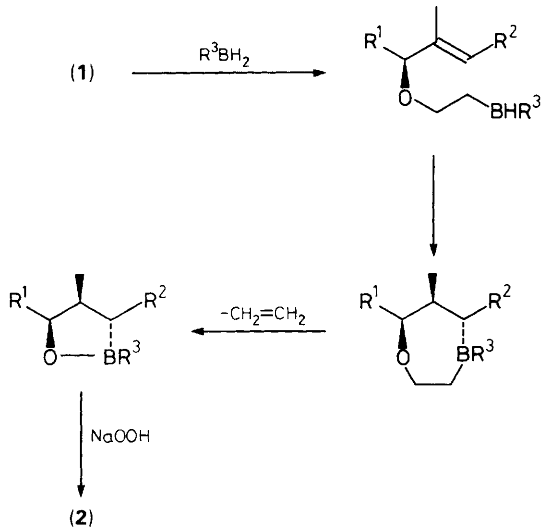
Stereoselective hydroborations of alkenes directed by pre-existing stereogenic centres have been frequently employed in natural product syntheses as useful methods for acyclic stereocontrol. Among those, secondary allylic alcohol derivatives $R^1CH(OX)CH(Me)=CH_2$ undergo highly selective hydroborations with bulky boranes to give *anti* 1,3-diol derivatives in general.[1] More recently, Evans and co-workers reported that a Rh^I-catalysed hydroboration of allylic alcohol derivatives proceeds with exceptional *syn* selectivity.[2] We wish to report here the first example of intramolecular hydroboration[3] of allylic alcohol derivatives which proceeds with *syn* selectivity opposite to that of the intermolecular counterpart.

As shown in equation (1), the reaction of allyl vinyl ether (**1a**—**e**) (R^2 = H) with $ThexBH_2$ (2.0 equiv.) in tetrahydrofuran (THF) (0.15—0.25 M) at temperatures from −85† to 20 °C for 18 h followed by standard treatment with alkaline hydrogen peroxide gave diol (**2a**—**e**) with almost exclusive *syn* selectivity in high yields (Table 1, entries 1—5). Hydroborations of (**1f**,**g**) (R^2 = Me) also proceeded with high selectivity while somewhat enforcing conditions [$ThexBH_2$ (1.0 equiv.) in refluxing THF] or employment of BH_3–THF (1.0 equiv.) were necessary for the intramolecular hydroboration step (*vide infra*) to be completed (entries 6—10).‡ It should be noted that the degree of selectivity in the present reaction is higher than those reported previously.[2,4]



(1)

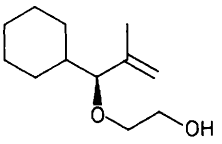
(**1a**—**g**) (**2a**—**g**)



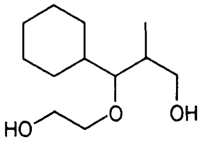
(2)

The following observations demonstrate that the present reaction proceeds through an intramolecular mechanism as shown in equation (2). Firstly, when the reaction mixture of (**1c**) (R^1 = cyclohexyl, R^2 = H) with $ThexBH_2$ was treated with alkaline hydrogen peroxide at −40 °C without warming to room temperature, the initial intramolecular hydroboration product (**3**) (12%) was obtained together with diol (**4**) (23%)§ and (**1c**) (39%). Secondly, on the other hand, the above reaction mixture, when oxidized after warming to −25 °C, gave diol (**4**) (80%)§ and a trace amount of diol (**2c**) (<1%). Thirdly, ethylene was detected by g.c. analysis before treatment with alkaline hydrogen peroxide in the reaction of entry 3.

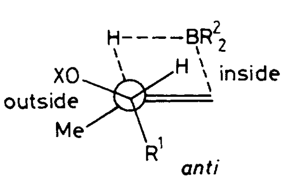
Recent theoretical studies on hydroborations by Houk and co-workers[5] provided us with information on the origin of the high *syn* selectivity observed in the present intramolecular hydroboration reactions. According to their calculations of the intermolecular hydroboration, *anti* diols are produced *via* a staggered transition state (**A**) where substituents R^1 and OX take *anti* and outside positions, respectively. They suggested the importance of stereoelectronic effect of the *anti* substituent which stabilizes the transition state in the increasing order of OX, H, and alkyl. Therefore, the *syn* selectivity in the



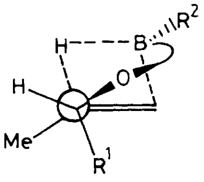
(**3**)



(**4**)



(**A**)



(**B**)

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† The temperature −85 °C is not critical in the present reaction; similar results were obtained when dry ice was used for cooling the reaction mixture. Authors usually use a Neslab Cryocool CC-80 immersion cooler in performing low temperature reactions.

‡ Reaction of (**1g**) with $ThexBH_2$ (1.0 equiv.) at 20 °C gave 2-(1-cyclohexyl-2-methylbut-2-enyloxy)ethanol (78%) as a major product.

§ Stereochemistry of (**4**) was not determined but its diastereo purity is over 95% judging from ^1H n.m.r. measurements.

Table 1. Intramolecular hydroboration of allyl vinyl ethers (**1**).

Entry	Substrate[a]		Borane (equiv.)		Cond.[b]	Product	Yield[c]	*syn* : *anti*[d]
1	(**1a**)	$R^1 = Bu^n, R^2 = H$	$ThexBH_2$	(2.0)	A	(**2a**)[e]	83%	>200 : 1
2	(**1b**)	$R^1 = Pr^i, R^2 = H$	$ThexBH_2$	(2.0)	A	(**2b**)[f]	83%	>200 : 1
3	(**1c**)	R^1 = Cyclo-hex, $R^2 = H$	$ThexBH_2$	(2.0)	A	(**2c**)[e]	90%	>200 : 1
4	(**1d**)	$R^1 = CH_2{=}C(Me){-}, R^2 = H$	$ThexBH_2$	(2.0)	A	(**2d**)[e]	81%	>200 : 1
5	(**1e**)	$R^1 = Ph, R^2 = H$	$ThexBH_2$	(2.0)	A	(**2e**)[e]	89%	16 : 1
6	(**1f**)	$R^1 = Bu^n, R^2 = Me$	$ThexBH_2$	(1.0)	B	(**2f**)[e]	30%	16 : 1
7	(**1f**)		BH_3–THF	(1.0)	A	(**2f**)	52%	30 : 1
8	(**1f**)		BH_3–THF	(2.0)	A	(**2f**)	66%	7.7 : 1
9	(**1g**)	R^1 = Cyclo-hex, $R^2 = Me$	$ThexBH_2$	(1.0)	B	(**2g**)[f]	39%	130 : 1
10	(**1g**)		BH_3–THF	(1.0)	A	(**2g**)	47%	39 : 1

[a] Prepared from the corresponding alcohol by treatment with refluxing ethyl vinyl ether in the presence of $Hg(OAc)_2$ (10 mol%). R. E. Ireland and D. D. J. Dawson, *Org. Synth.*, 1974, **54**, 71. [b] A; −85 °C → room temperature (18 h). B; −85 °C → room temperature (4 h), and then 66 °C (18 h). [c] Isolated yield. [d] Determined by capillary g.c. analysis of the bis-TMS (TMS = Me_3Si) ethers. [e] Identified by comparison with authentic *anti* diols prepared by the hydroboration of the parent allyl alcohol with $ThexBH_2$. [f] Determined by converting them to the acetal derivatives.

intramolecular hydroboration reactions is rationalized by the cyclic transition state (**B**) where R^1 takes the *anti* position. In the present reaction, high *syn* selectivity was observed irrespective of the bulkiness of substituent R^1 (*e.g.* entry 1 *vs.* 2 or 3) whereas the selectivity was somewhat lowered when R^1 is the less electron donating phenyl group (entry 5). These results suggest that the stereoelectronic effect, rather than simple steric effects, of substituent R^1 is important in determining the stereoselectivity.

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