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STUDIES ON THE STEREOSELECTIVE HYDROBORATION OF VINYL ETHERS

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ABSTRACT: The diastereoselective hydroboration/oxidation of several asymmetric vinyl ethers is presented.

The hydration of heteroatom-substituted olefins via hydroboration/oxidation holds considerable promise for the synthesis of functionalized carbon skeletons. For example, hydroboration of vinyl ethers (1) proceeds regiospecifically, by virtue of the highly polar nature of the substrate, to afford β-alkoxy boranes (2a and 2b) which yield 1,2-diol derivatives following oxidation (3a and 3b, figure 1.).[1] Unfortunately, β-alkoxy boranes such as 2a and 2b typically exhibit a pronounced tendency to undergo syn-elimination of the vicinal heteroatoms to result in deoxygenated olefins 4.[1,2] The degree to which this competing reaction participates is dependent upon several factors, including the nature of the substrate, the nature of the hydroborating agent, and the reaction conditions employed.

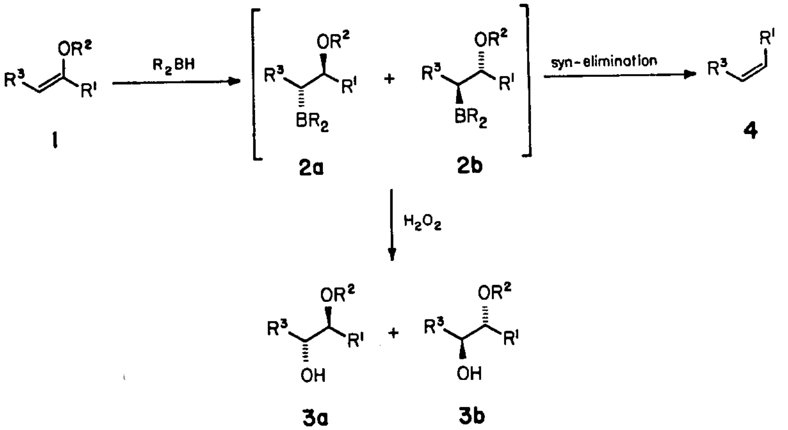
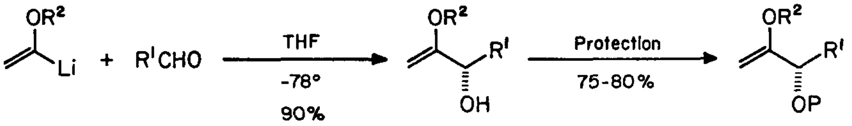


figure 1.

In view of the potential for the preparation of stereodefined polyols, we initiated a study into the hydroboration of vinyl ethers to examine the structural features in acyclic substrates 1 that affect the stability of intermediates 2 relative to 4 and to ascertain the degree to which diastereofacial bias (2a vs. 2b) may be influenced by allylic asymmetry.[3] For our preliminary studies, we prepared simple vinyl ether substrates 7 and 8 through routine methods by the condensation of vinyllithium species 5[4] with aldehydes 6. With a range of substrates readily available, a survey of a variety of



5 6 7 8

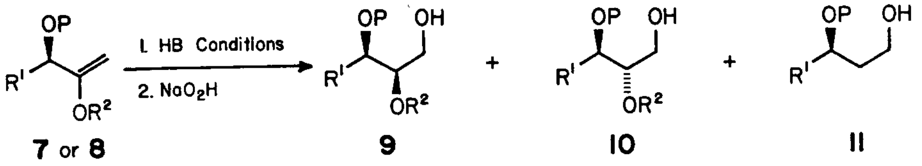
hydroborating agents including $BH_3 \cdot DMS$, $BH_3 \cdot THF$, $(Sia)_2BH$ (diisoamylborane), $ThBH_2$ (thexylborane), and 9-BBN (9-borabicyclo[3.3.1]nonane) in several solvents (DME, THF, CCl_4) was carried out. A portion of these results are represented in Table I.

Our efforts became focused on the BH_3 and $ThBH_2$ reagents when 9-BBN proved to be unreactive with these substrates and $(Sia)_2BH$ offered no advantages either in stereoselection or yields of the desired triols. Also, a comparative solvent study revealed no appreciable effects on the outcome of the reaction. Significantly, with few exceptions (see entries 14 and 15), elimination was not a serious competitive process and the desired triol derivatives were usually isolated in good to excellent yields. This undesirable side reaction intruded only when hydroboration was especially sluggish, usually with $ThBH_2$ treatment of the protected allylic alcohols. It should be noted that the behavior of these alkyl enol ethers (R_2 = alkyl) strongly contrasts with that reported for acyclic silyl enol ethers (R_2 = trialkylsilyl), which undergo facile β-elimination reactions.[1e,2c] The nature of the substitution on the allylic alcohol (P) appears to have little effect on the stability of the intermediate organoboranes.

Equally significant are the levels of diastereoselection attached to these hydration reactions. When simple BH_3 reagents are employed on unprotected substrates (P = H), modest selection for the syn isomers 9 is observed. On the other hand, protected vinyl ethers (P = protecting group) exhibited good to excellent levels of diastereofacial selection for the anti isomers 10 when treated with $ThBH_2$. Intermediate stereoselection is observed when protected and unprotected vinylic species were condensed with BH_3 and $ThBH_2$, respectively. The stereochemistry of the products was determined by ^1H NMR analysis of the cyclic borate esters (figure 2), the isomer possessing the larger coupling constant between the protons of the vicinal asymmetric centers being assigned to the anti isomer 10.

While information is lacking regarding the factors contributing to this "adjustable" stereoselectivity, we speculate that competition between transition states 12 and 13 may be important.[7] When the allylic alcohol is protected and the hydroborating reagent is sterically shielded, transition state 12 becomes favored to afford the anti product. Conversely, the combination of the unprotected alcohol and the sterically undemanding

TABLE I.



	R¹	R²[a]	P[a]	HB Conditions[b]	9:10[c]	Yield[d]	11
1	Ph	Et	H	BH_3·THF, THF, 0°, 3h	76:24	88%	—
2	Ph	Et	H	BH_3·DMS, DME, 0°, 3h	75:25	78%	—
3	Ph	Et	H	$ThBH_2$, THF, 0°→RT, 6h	26:74	93%	—
4	Ph	Et	BOM	BH_3·DMS, DME, 0°, 3h	75:25	84%	—
5	Ph	Et	MEM	BH_3·DMS, DME, 0°, 2h	60:40	89%	—
6	Ph	Et	TBS	BH_3·THF, THF, 0°, 3h	76:24	83%	—
7	Ph	Et	BOM	$ThBH_2$, THF, 0°, 2h	3:97	70%	—
8	Ph	Et	MEM	$ThBH_2$, THF, -20°, 1.25h	<5:>95	77%	—
9	Et	MOM	H	BH_3·DMS, THF, 0°, 3h	75:25	64%	—
10	tBu	MOM	H	BH_3·DMS, THF, 0°, 3h	63:37	61%	—
11	iPr	Et	H	BH_3·THF, THF, 0°, 2h	67:33	80%	—
12	iPr	MOM	H	BH_3·DMS, THF, 0°, 3h	87:13	73%	—
13	iPr	Et	H	$ThBH_2$, THF, 0°, 2h	20:80	93%	—
14	iPr	Et	BOM	$ThBH_2$, THF, -10°, 3h[e]	<5:>95	28%	20%
15	iPr	MOM	BOM	$ThBH_2$, THF, -5°, 4h[e]	12:88	24%	9%
16	iPr	Et	Ac	$ThBH_2$, THF, -5°, 4h	29:71	71%	—

[a] MOM = CH_2OCH_3, BOM = CH_2OCH_2Ph, MEM = $CH_2OCH_2CH_2OCH_3$, TBS = $tC_4H_9(CH_3)_2Si$. [b] In all cases, 3 equivalents of the borane reagent were used. [c] Ratios are determined by capillary GLPC analysis. [d] Isolated yield of purified triol products. [e] This reaction was not carried to completion due to competitive formation of 11.

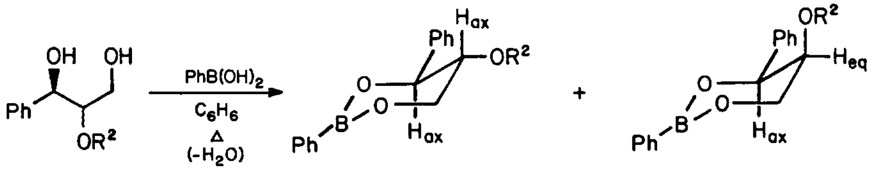
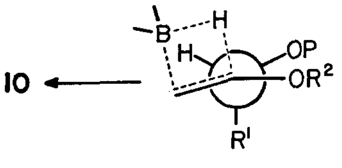


figure 2.

BH_3 may promote transition state 13, perhaps facilitated by a boron-oxygen interaction. Work is continuing to understand the mechanistic details of these stereoselective hydrations and to apply them to the synthesis of highly oxygenated natural products, including carbohydrates.



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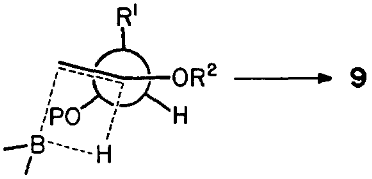

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