Tetrahedron Letters, Vol.30, No.4, pp 395-398, 1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

DIASTEREOCONTROL IN RHODIUM-CATALYZED HYDROBORATION OF CHIRAL ACYCLIC ALLYLIC ALCOHOL DERIVATIVES

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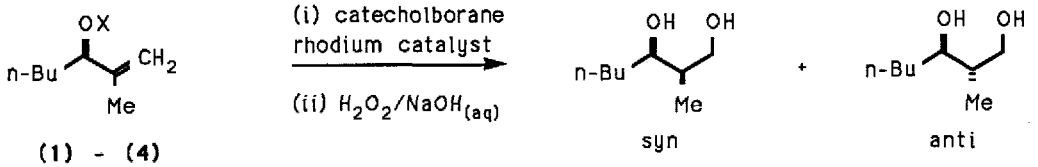
Abstract: Diastereoselectivities in rhodium-catalyzed hydroborations of the chiral allylic alcohol derivatives **(1)** - **(11)** are governed predominantly by electronic and "shape" factors.

Rhodium-catalyzed,[1] and "conventional",[2] hydroborations of alkenes clearly do not proceed via the same mechanism; consequently, there is no reason to assume similar chemo-regio-, and stereo- selectivities. Metal-catalyzed reactions therefore may eventually complement or supercede some of the hydroboration techniques that are used routinely at the present time. As a corollary to our work on *enantioselective* hydroborations mediated by homochiral rhodium complexes,[3] we are investigating catalyzed hydroborations of chiral substrates. Evans and co-workers recently communicated four examples of rhodium mediated hydroboration of acyclic allylic alcohol derivatives.[4] Consequently, we thought it appropriate to report our results in that area, extensive data that delineates the scope, limitations, and dominant factors influencing these particular reactions.

Initially we focussed on the following transformation because the corresponding uncatalyzed process has been investigated in detail.[5]



(1) - (4)

Entries 1 - 3 in Table 1 show that the free alcohol **(1)**[6] and the acetate **(2)** are hydroborated with moderate *syn* selectivities; the corresponding uncatalyzed hydroborations with dialkylboranes are *anti*-selective hence the methods are complementary

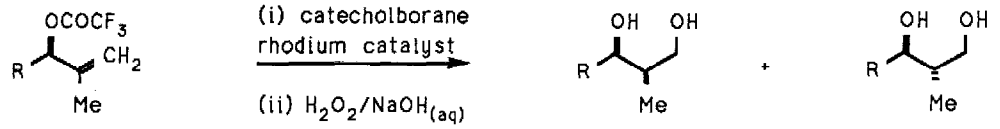
for these substrates. The *syn:anti* ratios for catalyzed hydroboration of ester **(2)** do not vary much over a 44° temperature range (entries 2 & 3). Carbamate **(3)** is hydroborated with comparable selectivity; we had imagined that transient coordination of the protecting group to the metal might alter the stereochemical bias in this example[7] but that is not the case. Remarkably, hydroboration of the trifluoroacetate **(4)** is approximately three times more diastereoselective than the corresponding reactions of substrates **(1)** - **(3)**. These results indicate there is a significant *electronic* effect influencing the stereochemical outcome of these reactions.

Table 1. Catalyzed Hydroboration of Substrates (1) - (4)[a]

Entry	Substrate	X	Temperature °C	Syn:Anti[b]
1	(1)	H	-4	2.2:1
2	(2)	Ac	-4	2.7:1
3	(2)	Ac	40[c]	2.4:1
4	(3)	$CONMe_2$	-4	2.4:1
5	(4)	$COCF_3$	-4	7.5:1

[a] THF, 48 h, with 1 mol % of $[Rh(COD)Cl]_2/PPh_3$ in a 1:4 ratio. [b] Work up with aqueous base gave near quantitative yields of the diols contaminated only with trace amounts of triphenylphosphine oxide derived from the catalyst (^1H NMR). The samples were derivatized without further purification. [b] Stereochemistries were assigned by comparison with authentic samples obtained in uncatalyzed hydroborations (9-BBN), ratios were determined by capillary GC analysis of acetonide derivatives. [c] Reaction time 12 h.

Settling then with trifluoroacetates, we investigated the influence of substrate structure, Table 2.



(5) - (10)

The series of compounds from **(5)** and **(6)** through to **(9)** and **(10)** was selected for study because the group R attached to the chiral center has a progressively greater steric influence on the reaction site. Esters **(5)** and **(6)** have large groups (^{i}Pr and Ph) well removed from the reaction center; these, like **(4)**, are hydroborated with high *syn* diastereoselectivities (entries 1 and 2). Surprisingly, hydroboration of substrates **(7)** and **(8)** corresponds to maximum *syn* selectivity in this series (entries 3 & 4).[8] When

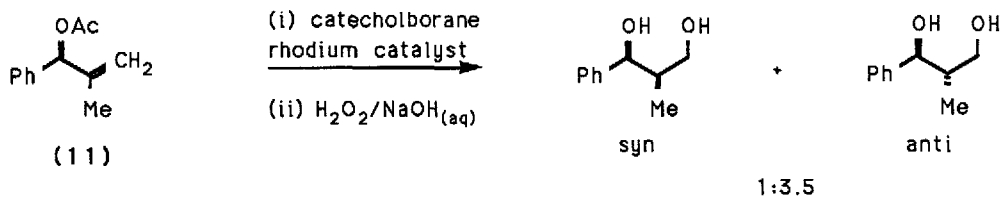
the ^{i}Pr group is directly attached to the chiral center (i.e. for substrate **(9)**, entry 5) the *syn* selectivity drops dramatically and the corresponding phenyl compound is hydroborated with slight *anti* selectivity (entry 6). These results indicate that substituent *shape is more important than size* when assessing diastereoselection in these reactions.[9]

Table 2. Catalyzed Hydroborations of Substrates (5) - (10)[a]

Entry	Substrate	R	Temperature °C	Syn:Anti[b]
1	**(5)**	^{i}PrCH$_2$CH$_2$	-4	5.8:1
2	**(6)**	PhCH$_2$CH$_2$	-4	6.9:1
3	**(7)**	^{i}PrCH$_2$	25	9.5:1
4	**(8)**	PhCH$_2$	25	14.2:1
5	**(9)**	^{i}Pr	25	3.6:1
6	**(10)**	Ph	25	1:1.5

[a] THF, 48 h, with 1 mol % of [Rh(COD)Cl]$_2$/PPh$_3$ in a 1:4 ratio. [b] Work up with aqueous base gave near quantitative yields of the diols contaminated only with trace amounts of triphenylphosphine oxide derived from the catalyst (^{1}H NMR). The samples were derivatized without further purification. [b] Stereochemistries were assigned by formation of acetonides and ^{1}H NMR analysis, ratios were determined by capillary GC of acetonide derivatives.

Catalyzed hydroboration of the acetate **(11)** is appreciably *anti*-selective.



In other work we have shown rhodium mediated hydroborations of this kind give similar yields and diastereoselectivities in THF, ether, and toluene but only starting material was recovered from our two attempts to run these reactions in dichloromethane. Reactions mediated by [Rh(COD)Cl]$_2$/PPh$_3$[10] are marginally more diastereoselective than those mediated by [Rh(COD)(PPh$_3$)$_2$][BPh$_4$][10] which in turn is a slightly more selective catalyst than [Rh(COD)(PPh$_3$)$_2$][PF$_6$][10]. The former catalyst system gives a neutral complex, the latter is a cationic complex and the tetraphenylborate salt is intermediate due to

coordination of the "counter ion" with the rhodium center.[11] Hydroborations catalyzed by neutral catalysts are faster than those mediated by their cationic counterparts.

The work presented here indicates stereoselectivities obtained in these reactions result from the interplay of several factors. Evans and co-workers implied that steric diastereoselectivities in catalyzed hydroborations of derivatives of alcohol **(1)** are determined by the bulk of the oxygen substituent. We have shown that other aspects of the substrate structure are significant, particularly electronic demands of the allylic functionality and the *shape* of groups attached to the chiral center.

Catalyzed hydroborations for syntheses of *syn*-2-methyl-1,3-diols are overshadowed by aldol methodology.[12] The true potential of catalyzed hydroborations of allylic alcohol derivatives is in manipulations of the intermediate boronate esters into functionalized compounds other than diols; such reactions are well established.[13] Furthermore, we have observed extremely high diastereoselectivities in rhodium mediated hydroborations of other chiral alkenes; details of this work will be reported in due course.

Acknowledgement: Financial support for this work was obtained from Rice University and The Robert Welch Foundation.

References and Notes

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6 The hydroxyl group of this substrate reacts rapidly with catecholborane to form a boronate ester.
7 For similar effects, see: J. M. Brown, Angew. Chem. Int. Ed. Eng., 1987, **26**, 190. The possibility that transient coordination occurs for substrates **(1)** - **(3)** and *not* for the trifluoroacetates is conceivable, though we think it unlikely.
8 Higher temperatures were required to drive reactions of the more hindered substrates to completion. We do not think this is important because diols isolated from the (incomplete) hydroboration of substrate **(9)** at -4 °C had almost the same *syn:anti* ratios as those formed in the experiments at 25 °C.
9 The steric influence of the substituents on the chiral center increases from **(5)** & **(6)** through to **(9)** & **(10)** but the diastereoselectivity is a maximum for **(7)** & **(8)**. This implies the catalyst is more sensitive to large groups slightly removed from the chiral center than to big substituents which are directly attached. Transient coordination of the phenyl groups and/or π-stacking effects are discounted because the ^{i}Pr an Ph substituted compounds follow the same trends with respect to diastereoselection.
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(Received in USA 20 October 1988)