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ON CATALYZED AND UNCATALYZED HYDROBORATIONS OF CHIRAL ALLYLIC ALCOHOLS AND AMINES

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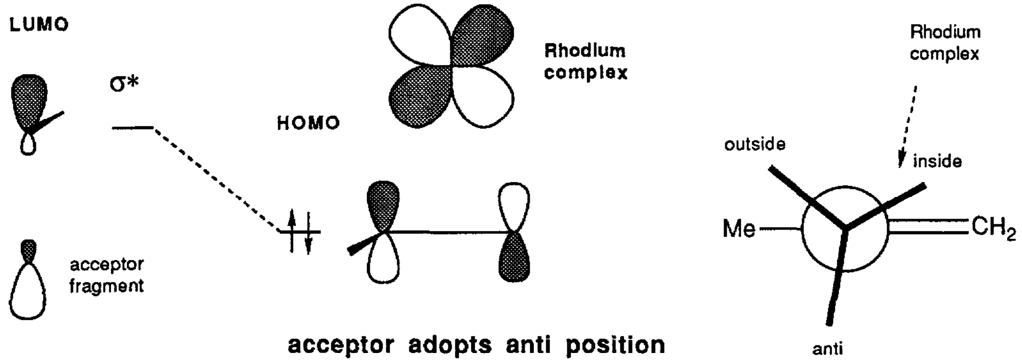
Abstract: A model for predicting the sense of diastereoselection in catalyzed hydroborations of allylic alcohol and allylic amine derivatives is discussed.

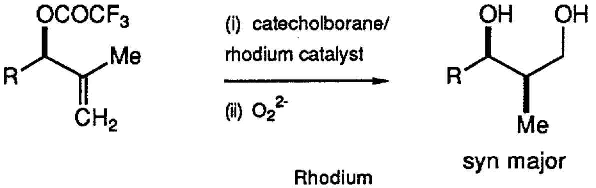
Substrate-controlled diastereoselective hydroborations of chiral allylic alcohols mediated by rhodium catalysts tend to give *syn* products whereas conventional (uncatalyzed) hydroborations of the same substrates are almost always *anti* *selective. Our investigations proved electronic effects are important in the catalyzed reactions so, for instance,* allylic acetates are hydroborated with less *syn* selectivity than allylic trifluoroacetates.[1] Results presented in the preceding paper in this issue demonstrate catalyzed and uncatalyzed hydroborations of allylic *amines* also can be "stereocomplementary". To date no rationale has been presented to account for these observations although there are several hypotheses to account for *anti* selectivity in conventional hydroborations of allylic alcohol derivatives.[2-4] We propose the model presented below rationalizes substrate-controlled diastereoselectivity in catalyzed hydroborations of chiral allylic alcohols and amines.

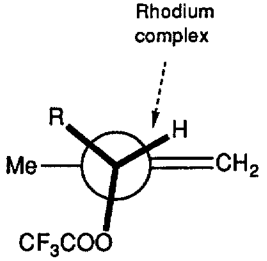


acceptor adopts anti position

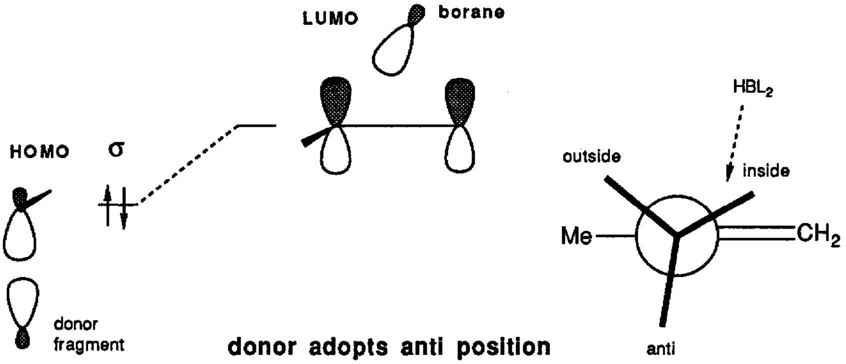
This theory depends on the following assumptions: (i) preferential approach of a rhodium complex on one diastereotopic face of the alkene substrates determines the stereochemical outcome of the catalyzed reactions and the major diastereomer formed reacts relatively rapidly to give the product;[5] (ii) the borane is delivered *endo* with respect to the metal; and, (iii) electronic effects are pivotal in determining the three dimensional trajectory of this interaction. If these basic tenets are sound, the substrate will react predominantly in a conformation which maximizes bonding between the frontier orbitals of the alkene and the metal. The catalysts are low oxidation state, electron-rich complexes so back-donation from the metal (Dewar-Chatt) is crucial. Therefore, ***the substrate will react in the conformation which best stabilizes electron density developing in the*** π^* ***orbital of the alkene fragment***, i.e. interactions will be between σ^* lobes of orbitals involved in bonding at the chiral center. σ-*Acceptor* groups have relatively low energy σ^*-orbitals available for mixing with the developing alkene/metal MO system hence we conclude that the best σ-acceptor will occupy the conformational position opposite to the approaching rhodium complex.

For instance, our model predicts that $OCOCF_3$ substituents (good σ-acceptors) will preferentially orientate *anti* to the approaching rhodium complex in catalyzed hydroborations of chiral allylic trifluoroacetates. The largest of the other two substituents on the chiral center will occupy the outside position and the smallest resides in the inside (crowded) site; consequently *syn* selectivity results.

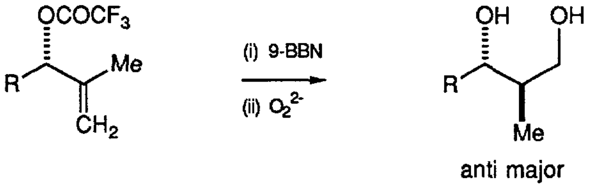


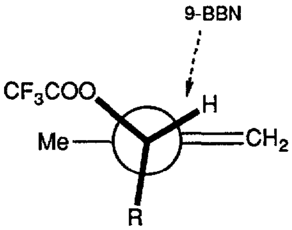


Houk's model for *conventional* hydroborations identifies overlap of a high energy σ-orbital with the LUMO formed via approach of the borane on the alkene as the crucial interaction (see below). A σ-*donor* therefore occupies the conformational position *anti* to the approaching borane.[6]



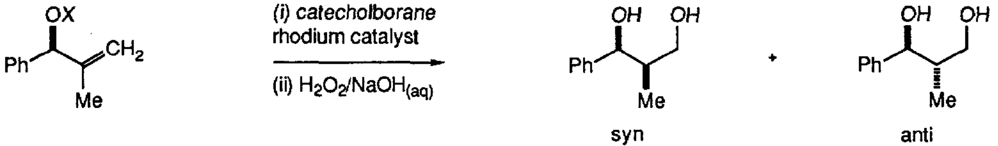
According to Houk, uncatalyzed hydroborations tend to be *anti* selective because the most reactive conformations are those with σ-donors *anti* to the approaching rhodium complex.





Complementary diastereoselectivities in catalyzed and uncatalyzed hydroborations therefore are predictable.

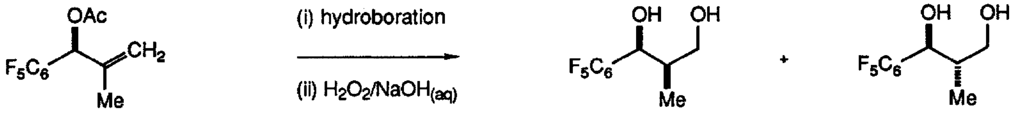
Our model implies that *syn* selection in catalyzed hydroborations should decrease as the σ-accepting character of the *anti* substituent decreases. This explains why catalyzed hydroborations of allylic trifluoroacetates are more *syn* selective than the corresponding reactions of allylic acetates and carbamates.[1] It also rationalizes the observation that cationic complexes are less diastereoselective in hydroborations of chiral allylic systems than neutral catalyst systems[1,7] because the latter have more electron density to shed via back-bonding. But what of those catalyzed processes which give slight *anti* selectivity? For instance, catalyzed hydroboration of the allylic acetate **(1a)** and of the corresponding trifluoroacetate **(1b)** are also *anti* selective.[1]



(1a) **X = $COCH_3$**
(1b) **X = $COCF_3$**

X	**syn:anti**
$COCH_3$	1.0:3.5
$COCF_3$	1.0:1.5

Preferential formation of *anti* products in both cases can be rationalized (at least in part) in terms of competition between the phenyl and acetate groups for the role of σ-acceptor. (Diminished *syn* selectivity (or, in this instance, increased anti selectivity) on substituting trifluoroacetate with acetate has already been explained.) To obtain further evidence we prepared and tested the pentafluorophenyl allylic acetate **(2)**. This structural modification lowers the σ*-orbital of the aryl ring relative to the phenyl derivative **(1a)** because the C_6F_5 substituent is a better σ-acceptor; consequently we predicted enhanced *anti* selectivity should result in the catalyzed hydroborations of this substrate. Conversely, our model suggests that uncatalyzed hydroborations of this substrate should be poorly *anti* selective or even *syn* selective. These predictions were confirmed experimentally as shown below.



(2) syn anti

conditions	**syn:anti**
2 eq. catecholborane, 1 mol % $[Rh(COD)Cl]_2.2$ PPh3, THF, 25 °C	1.0:6.9
4 eq. 9-BBN, THF, -78 to 25 °C then 48 h	1.0:3.0
4 eq. BH_3.THF, 0 to 25 °C then 6 h	1.5:1.0

The pentafluorophenyl substrate **(2)** gave predominantly *anti* product.in the catalyzed hydroboration whereas the uncatalyzed reactions were much less *anti* selective. To complete the study we also examined the uncatalyzed hydroborations of substrate **(1a)** and found 9-BBN gives a 4.5:1 *anti:syn* ratio (4 eq. 9-BBN, THF, -78 to 25 °C then 48 h) whilst borane gave slight *syn* selectivity (*anti:syn* = 1.0:1.5, 4 eq. BH_3.THF, 0 to 25 °C then 6 h). Thus the catalyzed hydroborations are more sensitive to electronic effects than the corresponding uncatalyzed reactions.

The theory presented in this paper is undeniably speculative and no provision for steric bulk of substituents, a factor which can be very important.[8] It certainly does not explain the curious dependance of diastereoselectivity on the three-dimensional "shape" of substituents attached to the chiral center as observed in a our study of catalyzed hydroborations of chiral allylic alcohols.[1,9] Nevertheless, the model provides a starting point for predicting the outcome of catalyzed hydroboration reactions and may only be superseded by intricate and involved mechanistic studies.

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References and Notes

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5 The mechanism of catalyzed hydroborations is unknown. Complexation of the metal could be reversible and the minor diastereomer of the complex formed could be more reactive; we assume this is not the case.
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7 See the preceding paper in this issue.
8 K. Burgess and M. J. Ohlmeyer, unpublished results.
9 We believe that this effect is due to the orientation of the substrate within the "catalyst pocket" of the complex, analogous to molecular shape recognition in enzyme-mediated reactions.

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