Substrate-Controlled Diastereoselectivities in Catalyzed and Uncatalyzed Hydroborations of Acyclic Allylic Alcohol Derivatives: Secondary Orbital Effects Involving dπ-pπ Interactions

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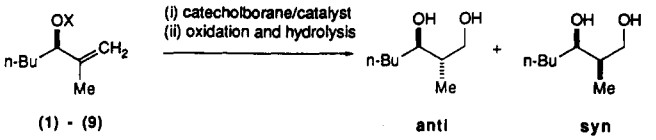
Rhodium-mediated hydroborations of allylic alcohol derivatives **1–9** followed by oxidation give predominantly *syn*-2-methyl 1,3-diols whereas conventional hydroborations of the same substrates afford mostly anti products. It is proposed that mixing of σ*-orbitals involved in bonding at the asymmetric center with π*-orbitals of the alkene lowers the LUMO involved in complexation of rhodium, and this could control diastereofacial selectivities in catalyzed hydroborations. Steric effects in catalyzed hydroborations are also discussed. The resulting hypotheses are tested with respect to catalyzed and uncatalyzed hydroborations of phenyl-substituted allylic alcohol derivatives **17–19** and $Ph(C_6F_5)CHCMe{=}CH_2$ (**21**) (a model substrate with aromatic groups of a similar size but different electronic properties attached to the chiral center). All experimental observations described here for catalyzed hydroborations of chiral alkenes are consistent with the proposals outlined above.

Additions of boron hydrides to alkenes and alkynes are among the most useful reactions in organic synthesis,[2-4] but still there is room for development. Boron hydrides are generally incompatible with amides (which are reduced)[5-7] and amines (which complex),[8-11] regioselectivities of nonterminal alkene and alkyne hydroborations are imperfect, and there is still not a general and convenient way to deliver B–H to alkenes with good control of absolute stereochemistry despite intense efforts with reagent-controlled diastereoselective hydroborations.[12-19] Certainly, there is no asymmetric hydroboration methodology that rivals the general utility of Sharpless' epoxidation[20-22] or Evan's enolates.[23,24] One might conclude that the chemistry of the alkyl–boron bond is extremely useful, but applications of this functionality are loosely confined within boundaries delineated by conventional hydroboration methodology, i.e. routes available to deliver B–H to unsaturation between carbon atoms.

Hydroboration of alkenes and alkynes via mechanisms which do not involve concerted addition of B–H bonds could overcome the restrictions outlined above. The first indications that such reactions exist came from several groups studying polyboron hydrides, who noted simple additions of these molecules to alkenes and alkynes can be accelerated by various transition-metal catalysts.[25-32] Pyrophoric, and relatively inaccessible, boron hydride

Table I. Catalyzed Hydroborations of Substrates 1–9[a]



(1) - (9) anti syn

entry	substrate	X	syn:anti[b]	source[c,d]
1	1	H	2.2:1.0	
2	2	Ac	2.7:1.0	
3	3	$COCF_3$	7.5:1.0	
4	4	CO^tBu	6.5:1.0	
5	5	THP	8.4:1.0	
6	6	CPh_3	18:1.0	
7	7	$^5BuMe_2Si$	24:1.0	*d*
8	8	$^tBuPh_2Si$	24:1.0	*d*
9	9	$CONMe_2$	2.4:1.0	

[a] THF, 48 h, with 1 mol % of $[Rh(COD)Cl]_2/PPh_3$ in a 1:4 ratio; workup with hydrogen peroxide/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 or by ^1H NMR analysis of acetonide derivatives; diastereomeric ratios determined by capillary GC analysis of acetonide derivatives. [c] This work unless otherwise indicated. [d] Evans and co-workers, see ref 39; catecholborane (3 equiv), 3 mol % $RhCl(PPh_3)_3$, 25 °C.

(1) Correspondence concerning the X-ray diffraction study should be addressed to this author.

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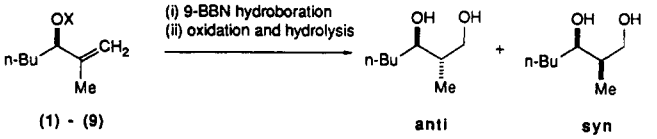
clusters, however, are not reagents of choice for organic chemistry. Consequently, the 1985 report[33] of appreciable rate enhancements for hydroborations of alkenes with *catecholborane* in the presence of rhodium(I) complexes was significant. Since then we,[34-38] and others,[39-43] have devoted attention to exploiting such *catalyzed* hydroborations in organic synthesis.

This paper focuses on control of relative stereochemistry in catalyzed hydroborations of chiral allylic alcohol derivatives. Results presented below indicate these reactions are "stereocomplementary" insofar as catalyzed hydroborations tend to form syn diastereomers preferentially whereas anti products result from the uncatalyzed processes. In analyzing factors which influence substrate-controlled diastereoselectivity in these reactions, we formulated a theory regarding secondary orbital interactions in $d\pi$-$p\pi$ bonding; this is presented here in the context of catalyzed hydroborations but may be applicable to other transition metal mediated reactions as well. Finally, model substrates designed to isolate electronic, from steric, effects have been hydroborated to test these hypotheses, and the results are summarized below.

Substrate-Controlled Diastereoselectivity in Catalyzed Hydroborations of Allylic Alcohol Derivatives. Table I presents diastereoselectivities observed in catalyzed hydroborations of a range of chiral allylic alcohol derivatives.[34] The strategy behind this study was to "tune" steric and electronic effects associated with the protecting group X and observe the stereochemical course of the reactions. Hydroboration of the acetate in entry 2 is moderately syn selective and provides a useful reference point to compare with other data. Replacing acetate with trifluoroacetate (entries 2 and 3) is essentially an electronic perturbation because the two protecting groups are around the same size; this change is associated with roughly a 3-fold increase in syn selectivity. Steric, rather than electronic, differences are dominant when comparing the acetate in entry 2 with the pivolate (entry 4) and, once again, a marked increase in syn selectivity is observed. The acetate in entry 2 differs from the tetrahydropyranyl (entry 5), and the trityl (entry 6), ethers mainly in terms of size; both protecting groups give enhanced syn selectivity and the increase for the trityl ether, the largest protecting group, is striking. Evans' results with siloxy ethers[39] (entries 7 and 8) combine the effect of extremely large protecting groups with powerful σ-acceptor capacities and optimum syn selectivities result. Finally, entry 9 was included as a probe for coordination effects; the Lewis basic nitrogen of the carbamate group might have acted as a ligand preferentially guiding the rhodium complex to one face of the alkene, evidently it does not.

Substrate-Controlled Diastereoselectivity in Uncatalyzed Hydroborations of Allylic Alcohol Derivatives. Experimental observations by Still et al.[44] provide an excellent comparison for the work reported above. We supplemented this study with two hydroborations of substrates not previously examined, and the collected results are shown in Table II. Anti selectivity is observed in every case, a marked contrast to the corresponding catalyzed reactions.

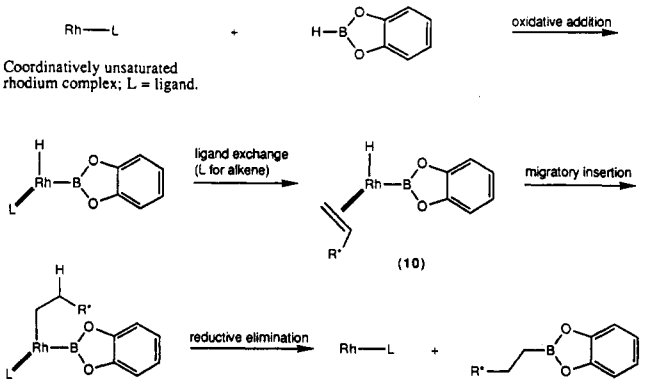
Table II. Uncatalyzed Hydroborations of Substrates 1–9[a]



entry	substrate	X	syn:anti[b]	source[c,d]
1	1	H	1.0:11	*d*
2	2	Ac	1.0:7.5	*d*
3	3	$COCF_3$	1.0:14	*d*
4	4	CO^{t}Bu	1.0:15.4	
5	5	THP	1.0:3.7	
6	6	CPh_3	1.0:5.5	*d*
7	7	^{t}BuMe$_2$Si	1.0:9.0	*d*
8	8	^{t}BuPh$_2$Si	1.0:6.0	*d*

[a] 9-BBN, THF, −78 °C to 25 °C; workup with hydrogen peroxide/aqueous base and purification via flash chromatography. [b] Stereochemistries were assigned by comparison with authentic samples or by ^{1}H NMR analysis of acetonide derivatives; diastereomeric ratios determined by capillary GC analysis of acetonide derivatives. [c] This work unless otherwise indicated. [d] Still and coworkers, see ref 44.

Scheme I. Generalized Mechanism for Catalyzed Hydroborations



Mechanistic Considerations. Scheme I depicts a resonable mechanism for hydroborations of alkenes with catecholborane in the presence of a rhodium(I) catalyst. The first step involves activation of catecholborane and is consistent with previous reports implicating oxidative additions of B–H bonds to coordinatively unsaturated metal centers.[45-51] The pathway presented here is also consistent with Noth's observation that oxidative addition of catecholborane to rhodium complexes gives a complex which reacts with alkenes to give hydroboration products.[33] However, attempts by us and Marder et al.[52] to follow this reaction by ^{31}P NMR proved that more than one complex is formed under the catalytic conditions, and the situation

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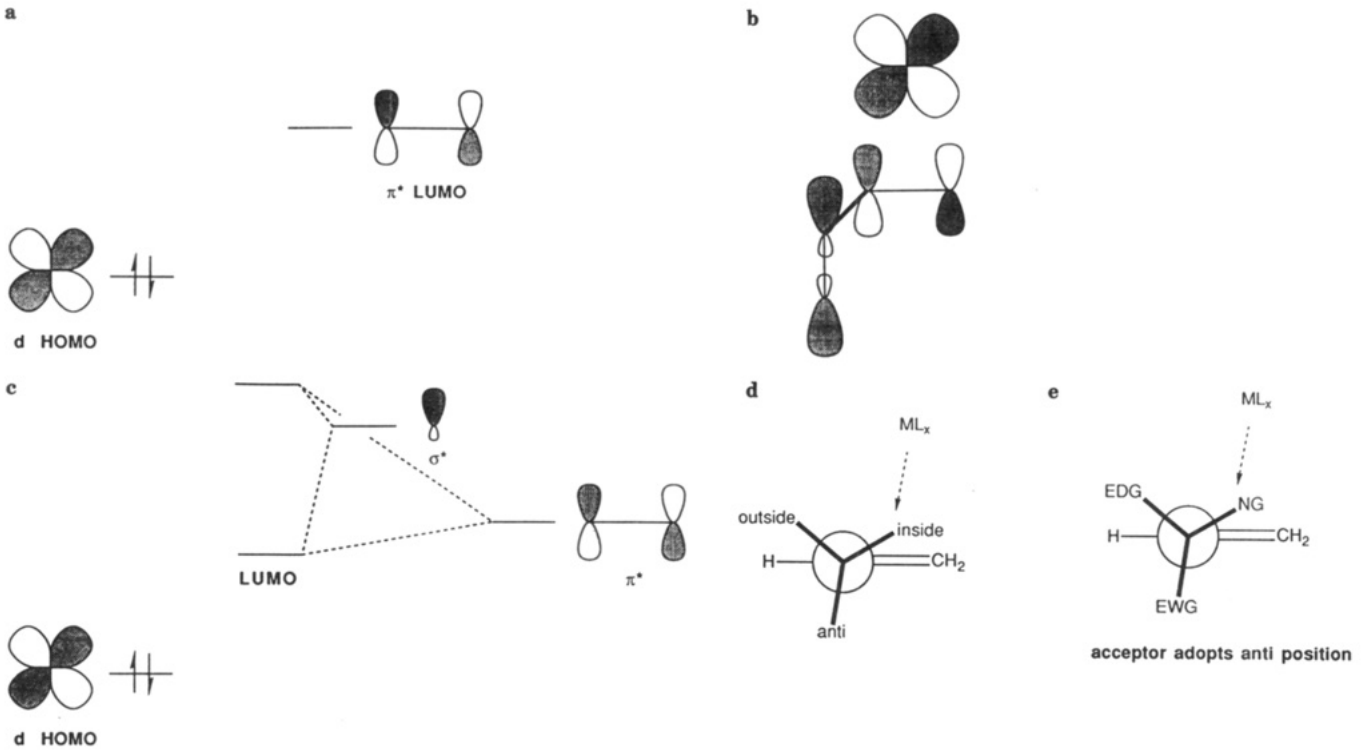


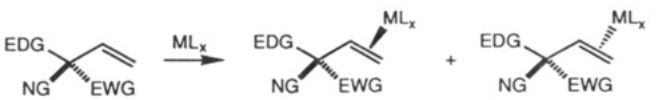
Figure 1. (a) Primary interaction in coordination of a chiral allylic alkene to a transition metal complex. (b) Orbitals involved in the primary and secondary interactions. (c) Secondary interaction in coordination of a chiral allylic alkene to a transition-metal complex lowers the LUMO level relative to the primary interaction alone. (d) Orientation of groups in the reactive conformation. (e) Preferential orientation based on electronic demands of the substituents.

is complicated by disproportionation of catecholborane.

Other mechanisms for catalyzed hydroborations that are not encompassed by Scheme I are conceivable. For instance, the coordinated alkene of complex **10** may insert into the rhodium–boron bond rather than into the rhodium–hydride linkage; however, we do not believe this is so because it would require formation of a secondary alkyl complex to account for the overall regiochemistry of the hydroboration. Mechanisms which deviate further from Scheme I we regard as even less plausible.

Applying the mechanism shown in Scheme I leads to the following conclusion: *if the major diastereomer of complex type 10 forms irreversibly and/or reacts relatively quickly to give the product, diastereoselection for catalyzed hydroborations of allylic alcohol derivatives **1–9** will be determined via the diastereofacial selectivity of coordination to the alkene.* The assumption implicit in this statement is product formation does not proceed predominantly via an equilibrium including a minor diastereomer which reacts quickly, i.e. the peculiar situation observed for rhodium-catalyzed hydrogenation of dehydroamino acids[53–56] is *not* applicable. A deuterium labeling study including a catalyzed reaction of catecholborane-D_1 ($C_6H_4O_2BD$) with a 1,1-disubstituted alkene/alcohol similar to substrates **1–9** has been performed,[43] and when this reaction was stopped before completion deuterium was not detected in the starting material, only in the product. Evans and coauthors state this observation implies, "... binding of the catalyst is not highly reversible for this olefin", an assertion which supports the assumption described above. In fact, all the trends presented below and in the following paper suggests π-complexation in catalyzed hydroborations of substrates **1–9** is critical in determining diastereoselectivities of these reactions.

Secondary Orbital Effects Involving dπ-pπ Interactions. Consider approach and bonding of a transition-metal complex, ML_x, to an alkene (**11**) which has electron-withdrawing (EWG), electron-donating (EDG), and neutral (NG) groups bonded to an α-chiral center. Initially, assume the substituents EWG and EDG are large and of identical size while NG is smaller. Two diastereomers **12** and **13** form when a metal π-bonds to the alkene, and relative amounts of these define the diastereofacial selectivity of the complexation.



(11) **(12)** **(13)**

The weakest bond in this π-complexation arises from back-donation of electron density from a filled d orbital on the metal to a π*-orbital of the alkene (Dewar–Chatt bonding, Figure 1a). Stereoselectivity in this reaction will arise if there is a reactive conformation of the alkene which corresponds to net stabilization of this incipient bond. We propose such conformations result from mixing σ*-orbitals associated with bonds at the chiral center with the π*-orbital of the alkene (Figure 1b); this facilitates increased back-bonding due to diminished HOMO–LUMO energy differences (Figure 1c). Thus the secondary interaction reinforces the primary interaction by creating an orbital which is closer in energy to the metal d orbital than the unperturbed alkene π*-orbital. Given the electronic hierarchy defined above, which substituent (EWG, EDG, or NG) will preferentially orient in the crucial anti position where the σ*-orbital can overlap with the alkene π* (Figure

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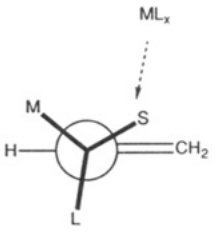
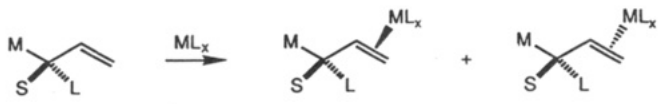


largest group adopts anti position

Figure 2. Preferential orientation based on steric demands of the substituents.

1d)? It will be the best σ-acceptor, EWG, because this has the lowest energy σ^*-orbital, i.e. the one most energetically compatible with the alkene π^*-orbital. Consequently, when predicting the diastereofacial selectivity of a reaction such as this, one should place the best σ-acceptor in the anti position and the smallest group (NG) in the "inside crowded" position (the sterically most congested site due to the approach of the metal, vide infra) (Figure 1e). Diastereomer **12** therefore should be formed in preference to **13**.

Substrate-controlled diastereoselectivity usually involves electronic *and steric* factors; however, it is convenient to consider these separately. Below is a model reaction in which the same metal fragment, ML_x, approaches and bonds to an α-chiral alkene **14** with (electronically identical) large (L), medium (M), and small (S) substituents.

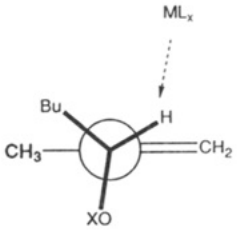


(14) **(15)** **(16)**

For reactions which do not involve metals, the largest group tends to orientate away from (or anti to, Figure 1d) the approaching reagent,[57] similar factors should place the largest substituent in the anti position in these complexation reactions. The next largest substituent (M) will preferentially adopt the "outside" position which is less encumbered than the "inside crowded" site, a position best suited to the smallest substituent (S) (Figure 2).

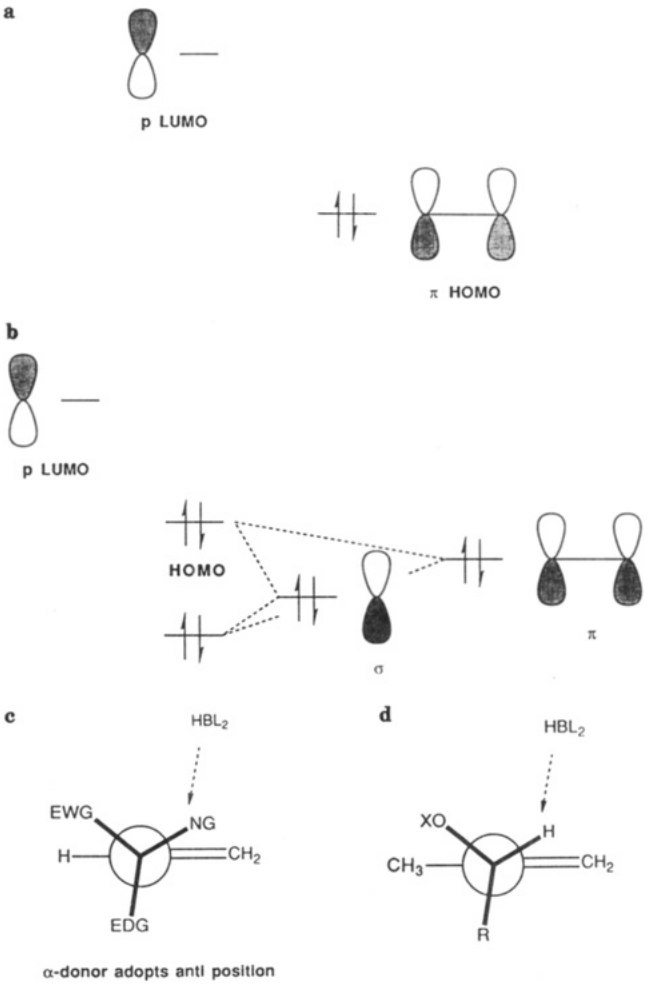
In reality most α-chiral alkene substrates have substituents with different steric and electronic demands, so both models should be applied. When the electronic and steric effects are working in opposition, the models predict the selectivity should be less than optimum; however, they are of little value beyond this unless there is empirical evidence concerning the relative magnitude of the steric and electronic contributions. Conversely, electronic and steric effects reinforce each other when the best σ-acceptor is also the largest substituent, and good diastereofacial selectivity should result. Thus we predict *diastereoselection in catalyzed hydroborations of allylic alcohol derivatives will be optimum if the protected alcohol is a good σ-acceptor and is large, relative to the other substituents on the asymmetric center.* In that case we propose the OX substituent adopts a position near perpendicular to the alkene and directs in the metal to the opposite face of the alkene as indicated in Figure 3.

Review of Table I shows the hypothesis presented above is consistent with the observed selectivities. Taking the acetate in entry 2 as a basis for comparison reveals syn selectivity is directly related to electronic effects (tri-



large acceptors adopt anti position

Figure 3. Preferential orientation in catalyzed hydroborations of allylic alcohols **1–9** based on combined electronic and steric demands.



α-donor adopts anti position

Figure 4. (a) Primary interaction in an uncatalyzed hydroboration of a chiral allylic alkene. (b) Secondary interactions in uncatalyzed hydroborations of a chiral allylic alkene enhances incipiant bonding by destabilizing the HOMO. (c) Preferential orientation based on electronic demands of the substituents. (d) Preferred reactive conformation in uncatalyzed hydroborations of allylic alcohol derivatives.

fluoroacetate, entry 3) and to steric effects (pivolate, tetrahydropyranyl, and trityl, entries 4–6). Furthermore, maximum syn diastereoselection results when the two effects are combined (entries 7 and 8).

Houk's studies[58] indicate the primary interaction in *uncatalyzed* hydroborations is that between the empty borane p orbital and the filled π-orbital of the alkene as depicted in Figure 4a. This is enhanced by a secondary interaction between a σ-orbital from the asymmetric center

(57) Houk, K. N.; Paddon-Row, M. N.; Rondan, N. G.; Wu, Y.; Brown, F. K.; Spellmeyer, D. C.; Metz, J. T.; Li, Y.; Loncharich, R. J. *Science* **1986**, *231*, 1108.

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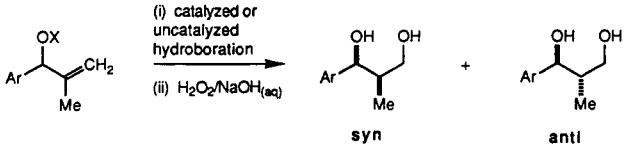
Table III. Catalyzed Hydroborations of Substrates 17–19[a]



entry	catalyzed[a] uncatalyzed[b]	substrate	X	Ar	syn:anti[c]
1	catalyzed	17	$COCF_3$	Ph	1.0:1.5
2	catalyzed	18	Ac	Ph	1.0:3.5
3	uncatalyzed	18	Ac	Ph	1.0:4.5
4	catalyzed	19	Ac	C_6F_5	1.0:6.9
5	uncatalyzed	19	Ac	C_6F_5	1.0:3.0
6	uncatalyzed[d]	19	Ac	C_6F_5	1.5:1.0

[a] THF, 48 h, with 1 mol % of $[Rh(COD)Cl]_2/PPh_3$ in a 1:4 ratio; workup with hydrogen peroxide/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] 9-BBN, THF, −78 °C to 25 °C; workup with hydrogen peroxide/aqueous base and purification via flash chromatography. [c] Stereochemistries were assigned by ^1H NMR analysis of acetonide derivaties; diastereomeric ratios determined by ^1H NMR analyses of the crude reaction mixtures after oxidation. [d] BH_3·THF in THF, 0–25 °C; workup with hydrogen peroxide/aqueous base and purification via flash chromatography.

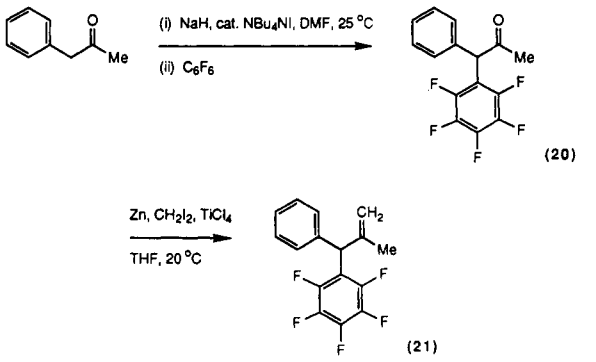
and the alkene π-orbital, which destabilizes the HOMO to promote overlap with the LUMO (i.e. the borane p orbital) thereby accelerating the overall reaction (Figure 4b). This secondary interaction will be maximum when the σ-level is energetically close to the alkene π-orbital, i.e. when an electron-donating group occupies the anti position (Figure 4c). Figure 4d illustrates the model that should apply to uncatalyzed hydroborations of allylic alcohol derivatives **1–9**, correctly predicting anti selectivity in these reactions.

Substrate-Controlled Diastereoselectivity in Hydroborations of Other Substrates. The hypotheses presented above are consistent with results presented in Table I and those observed in hydroborations of protected allylamine derivatives (described in the following paper). However, experiments proved catalyzed hydroborations of some phenyl-substituted allylic alcohols are anti selective (Table III), which, on first consideration, seems contradictory.

Steric effects partially account for this reversal in stereoselectivity (cf. Table I); a phenyl group is larger than a butyl hence it competes more effectively with the "OX" substituent for the critical anti position. However, electronic factors also favor anti selectivity in catalyzed hydroborations of these substrates because a phenyl group is a better σ-acceptor than a butyl group. Consequently, catalyzed hydroboration of the phenyl-substituted trifluoroacetate (entry 1) is less anti selective (or more syn selective) than hydroboration of the corresponding acetate under the same conditions because trifluoroacetate is a better σ-acceptor. To test this explanation we hydroborated the pentafluorophenyl-substituted alkene **19**, reasoning fluoride substitution enhances the σ-acceptor capacity of an aromatic ring hence anti selectivities in catalyzed hydroborations of these substrates should increase. Entry 4 shows this is so, and entries 5 and 6 prove fluorination has the opposite effect on the corresponding uncatalyzed hydroborations, as expected.

Finally, in an effort to isolate electronic effects in these reactions, model substrate **21** was prepared (Scheme II) and hydroborated; the diastereomeric alcohols formed in these reactions are separable via flash chromatography.[59]

Scheme II. Preparation of α-Chiral Alkenes with Electronically Different Substituents



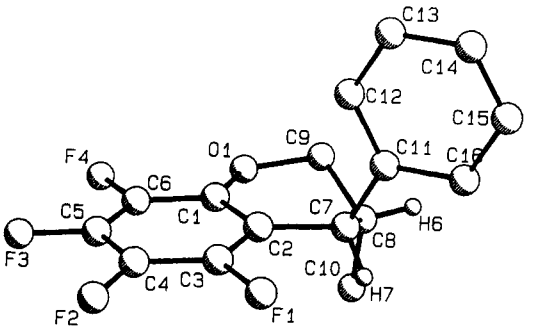
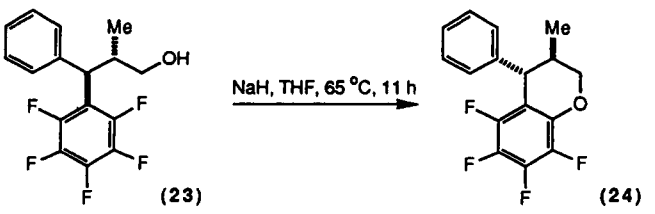


Figure 5. An abbreviated PLUTO diagram of the cyclic derivative **24**.

Table IV. Selected Bond Distances and Angles for Cyclic Derivative 24

	Distances (Å)		
C1–C2	1.39 (1)	C2–C3	1.36 (1)
C3–C4	1.39 (1)	C4–C5	1.34 (1)
C5–C6	1.36 (1)	C6–C1	1.40 (1)
C1–O1	1.344 (9)	C2–C7	1.51 (1)
C7–C8	1.55 (1)	C8–C9	1.50 (1)
C9–O1	1.44 (1)		
	Angles (deg)		
C1–C2–C7	120.3 (7)	C2–C7–C8	107.8 (7)
C7–C8–C9	109.5 (8)	C8–C9–O1	111.1 (7)
C9–O1–C1	116.2 (6)	H6–C8–C7	107.13
H7–C7–C8	107.07	C11–C7–C8	114.4 (7)
C10–C8–C7	113.5 (6)		
	Torsion Angle (deg)		
H6–C8–C7–H7	79		

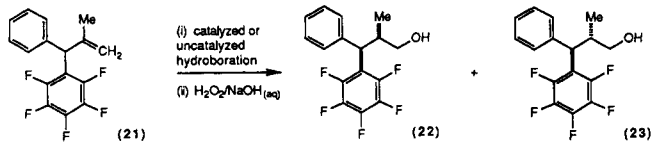
One pure diastereomer was treated with base to force intramolecular cyclization via nucleophilic displacement of fluoride from the pentafluorophenyl group, in an effort to assign relative stereochemistries via formation of a cyclic derivative. The cyclic product so produced (**24**) was not



amenable to unambiguous stereochemical assignments via NMR spectroscopy,[38] hence it was analyzed by single-crystal X-ray diffraction. The solid-state structure of this

(59) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

Table V. Catalyzed and Uncatalyzed Hydroborations of Substrate 21[a]



entry	conditions	syn:anti[b] 22:23
1	2 catecholborane, 1 mol % $[Rh(COD)Cl]_2$, 4 mol % PPh_3, 25 °C	2.5:1.0
2	2 catecholborane, 2 mol % $[RhCl(PPh_3)_3]$, 25 °C	1.9:1.0
3	2 9-BBN, −25 °C	1.0:1.5

[a] All reactions were performed in THF for 48 h (catalyzed reactions) and 72 h (uncatalyzed). [b] Product ratios determined via HPLC analysis of crude reaction mixtures.

molecule is represented in Figure 5 and important bond parameters are shown in Table IV; consequently, relative stereochemistries of diastereomers **22** and **23** formed in the hydroboration reactions were deduced to be as illustrated in Table V. Catalyzed hydroboration of substrate **21** is stereocomplementary to its uncatalyzed hydroboration with 9-BBN. Preferential formation of syn alcohol **22** in the catalyzed hydroborations (entries 1 and 2) is consistent with reaction via a reactive conformation in which the pentafluorophenyl group is oriented anti to the approaching metal with the hydrogen substituent occupying the inside (crowded) position, experiments which support the theory of secondary interactions in d-π^* bonding as presented above.

Conclusions. Secondary orbital interactions involving $d\pi$-$p\pi$ bonds provide a meaningful rationale for the stereocomplementary nature of catalyzed and uncatalyzed hydroborations. Catalyzed hydroborations of α-chiral allylic alcohols tend to be syn selective whereas conventional hydroborations of the same substrates tend to be anti selective. The origin of this behavior is explicable in terms of combined steric and electronic effects recognizing the electronic requirements for formation of a bond between a borane and an alkene are different when B–H bonds are delivered via a metal as opposed to direct addition. Other factors certainly influence the catalyzed reactions; for instance, we have observed unusual steric effects for hydroborations of different alkyl-substituted allylic alcohol derivatives.[36] Nevertheless, the hypotheses presented here have predictive value; diastereoselection in catalyzed hydroborations of α-chiral alkenes should be high when one of the substituents on the asymmetric center is relatively large and a good σ-acceptor.

Secondary orbital interactions of the type outlined above could influence any reaction involving transient coordination of a transition metal to an alkene. Conjugate additions of cuprates to γ-alkoxy-α,β-unsaturated derivatives[60] may also be controlled, at least in part, by stereoelectronic effects of the kind outlined above, and others have mentioned d,π^*-complexation in anti S_N2' displacements of allylic leaving groups by cuprates.[61,62]

Experimental Section

General Procedures. Melting points were determined on a Mel-Temp capillary melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded as liquid films (or $CHBr_3$ solutions for the solids) on a Perkin-Elmer 1600 Series FTIR or a Beckman 4200 Series spectrophotometer. Low-resolution (EI) and high-resolution (EI) mass spectra were determined on a Finnigan 3300 mass spectrometer and a CAC 21/110 C high-resolution mass spectrometer, respectively. HPLC was performed on a Rainin HPLC pump and a 4.6 mm × 25 cm 60-Å pore size silica column (Rainin Si 83-101-C) with an ISCO V4 UV-visible detector interfaced with an Apple Mcintosh plus. Gas chromatography was performed on a Shimadzu GC-9A with a 50 m 007 methyl phenyl (5%) silicone 0.25 mm i.d. 0.25 μm film thickness fused silica capillary column (Quadrex cat. no. 007-2-50-0.25F). High-field NMR spectra were recorded on a Bruker AF300 (^{1}H at 300 MHz, ^{13}C at 75.4 MHz) or a Bruker AC250 (^{1}H at 250 MHz, ^{13}C at 62.5 MHz, ^{19}F at 235.4 MHz) instrument in $CDCl_3$ unless otherwise stated. ^{1}H chemical shifts are reported in δ ppm relative to $CHCl_3$ (7.25 ppm) or TMS (0.0 ppm) as an internal reference, and ^{13}C chemical shifts are reported in δ ppm relative to $CDCl_3$ (77.0 ppm) as an internal reference. ^{19}F chemical shifts are reported relative to $CFCl_3$. In cases were abbreviated DEPT sequence experiments were carried out during ^{13}C NMR experiments, the carbon multiplicities are listed as (C) quaternary, (CH_2) methylene, and (CH/CH_3) methine/methyl. Thin-layer chromatography was performed on silica gel 60 F_{254} plates from Whatman. Flash chromatography was performed on SP silica gel 60 (230–400 mesh ASTM). Tetrahydrofuran (THF) was distilled immediately before use from sodium benzophenone ketyl. Borane–THF complex and 9-BBN solutions were purchased from Aldrich Chemical Co. and used as received. Catecholborane was purchased from Aldrich and distilled under reduced pressure before use. Organic solutions were dried over magnesium sulfate.

General Procedure for Catalyzed Hydroborations of Alkenes 1–9. A Schlenk tube was charged with 4.9 mg (0.01 mmol) of chloro(1,5-cyclooctadiene)rhodium(I) dimer and 11.0 mg (0.041 mmol) of triphenylphosphine, evacuated, and flushed with argon five times. THF, 1.0 mL, was added, and the bright yellow solution was stirred at 25 °C for 5 min. The substrate, 1 mmol, was added followed by a further 2 mL of THF, and the mixture was then cooled to −78 °C. Catecholborane 0.24 g (2 mmol, 2 equiv) was added then the mixture was stood at −4 °C for 48 h. At 0 °C, 1 mL of 95% ethanol, 3 mL of 3 M sodium hydroxide, and 1 mL of 30% hydrogen peroxide were added, and the mixture was stirred at 25 °C for 12 h. The mixture was diluted with 15 mL of 1 M sodium hydroxide and then extracted 3 × 50 mL of ether. The combined extracts were washed with 20 mL of 1 M sodium hydroxide and then 20 mL of saturated aqueous ammonium chloride and dried. Evaporation of the solvent gave the crude diol for 1–4. 90-MHz ^{1}H NMR spectra showed traces of triphenylphosphine oxide as the only contaminant.

For determinations of diastereomeric excesses, the acid labile protecting groups on **5** and **6** were removed by stirring the crude material in 5 mL of 95% ethanol with 1 drop of concentrated aqueous HCl for 12 h. Ether (50 mL) was added, and the organic layer was washed with 10 mL of saturated aqueous $NaHCO_3$ and dried. Acetonides of the crude diols were formed by stirring with 2,2-dimethoxypropane (0.7 g, 0.6 mL, 5 equiv) in 3 mL of ether with catalytic *p*-toluenesulfonic acid for 12 h and then diluting with 20 mL of ether. The ether solution was washed with 10 mL of saturated aqueous sodium bicarbonate and dried. The acetonides were pure by GC.

2-Methyl-1-(pentafluorophenyl)-2-propen-1-ol Acetate (19). Magnesium, 0.53 g (22 mmol), was placed in a two-neck round-bottomed flask equipped with a septum and a reflux condenser. A crystal of iodine was added, the apparatus was flushed with nitrogen; 5 mL of ether was added, and then bromopentafluorobenzene, 4.94 g (20 mmol), was added slowly with further ether to maintain a steady exothermic reaction. The total volume of ether added was 40 mL. After the addition of bromopentafluorobenzene was complete, the mixture was stirred at 25 °C for 15 min and then cooled to 0 °C. Methacrolein, 1.4 g (1.65 mL, 20 mmol), was added, and the mixture was stirred at 25 °C for 12 h and cooled to 0 °C, and 20 mL of saturated aqueous ammonium chloride was added. The solution was diluted with 150 mL ether, and the aqueous layer was separated. The ether layer was washed with 50 mL brine and dried. Evaporation of the solvent gave the crude material, which was distilled 45–50 °C (1 mmHg) to give 3.47 g (14.7 mmol) 73% of the alcohol,

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(61) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1984**, *25*, 3063.
(62) Marshall, J. A. *Chem. Rev.* **1989**, *89*, 1503.

2-methyl-1-(pentafluorophenyl)-2-propen-1-ol, which was used without further characterization. 90-MHz NMR: 1.72 (s, 3 H), 2.38 (d, J = 7.0 Hz, 1 H), 5.02 (s, 1 H), 5.10 (s, 1 H), 5.44 (d, J = 7.0 Hz, 1 H).

2-Methyl-2-(pentafluorophenyl)-2-propen-1-ol, 4.45 g (18.7 mmol, as prepared above), was dissolved in 30 mL of ether with catalytic DMAP, and acetic anhydride, 2.3 g (22 mmol), was added; this mixture was stirred at 25 °C for 10 h. The solution was diluted with 100 mL ether, washed with 2 × 50 mL of water and then 1 × 50 mL of saturated aqueous sodium bicarbonate, and dried. Evaporation of the solvents gave the crude acetate which was distilled at 83 °C (1 mmHg): 250-MHz ^{1}H NMR 1.74 (s, 3 H), 2.11 (s, 3 H), 5.02 (s, 1 H), 5.05 (s, 1 H), 6.38 (s, 1 H); ^{13}C NMR 18.7, 20.43, 68.83, 113.23, 139.46, 169.62; ^{19}F NMR −141.5, −145.5, −162.3; IR 3100 (w), 2980 (w), 2970 (w), 1750 (st br), 1655 (st), 1510 (st br), 1445 (m), 1370 (st), 1300 (m), 1220 (st br).

Catalyzed Hydroboration of 2-Methyl-1-(pentafluorophenyl)-2-propen-1-ol Acetate (19). Synthesis of *anti*-2-Methyl-1-(pentafluorophenyl)-1,3-propanediol. The acetate of 2-methyl-1-(pentafluorophenyl)-2-propen-1-ol was hydroborated using the procedure for 1–9 to give 0.252 g, 98%, of the crude diol as a 1.0:6.9 syn:anti mixture: ^{1}H NMR 0.69 (d, J = 7.0 Hz, 3 H), 2.34 (m, 1 H), 3.20 (br s, 1 H), 3.72 (dd, J = 7.6, 10.9 Hz, 1 H), 3.72 (dd, J = 3.6, 10.9 Hz, 1 H), 4.40 (br s, 1 H), 4.94 (d, J = 9.8 Hz, 1 H); ^{13}C NMR 13.0 (CH/CH$_3$), 67.4 (CH$_2$), 70.9 (CH/CH$_3$); MS m/e (%) 256 (M$^+$, <1), 248 (3), 192 (100).

1-(Pentafluorophenyl)-1-phenyl-2-propanone (20). Sodium hydride, 4.1 g (86 mmol) of a 50% dispersion in oil, was placed in a 2-neck round-bottomed flask against a stream of argon and washed three times with hexane. Tetra-*n*-butylammonium iodide (0.2 g) was added followed by 40 mL of dry DMF, and the mixture was stirred vigorously to suspend the sodium hydride. Hexafluorobenzene, 8.0 g (4.9 mL, 43 mmol), was added, the mixture was cooled to 0 °C, and then 6.0 g (43 mmol) of 1-phenyl-2-propanone was added in one portion, at 0 °C, with vigorous stirring. The mixture was stirred at 25 °C for 18 h, during which time a deep red color developed, and then it was poured onto 100 mL of ice-cold 1 M hydrochloric acid. The mixture was extracted with 3 × 100 mL of ether, and the combined extracts washed with 3 × 50 mL of 0.5 M hydrochloric acid. The ether solution was dried over magnesium sulfate and concentrated to give the crude material as a pale yellow mobile oil. Flash chromatography eluting with 5% ethyl acetate in hexane gave 5.7 g (19 mmol), 44%, of the product: 90-MHz ^{1}H NMR 2.24 (s, 3 H), 5.20 (s, 1 H), 7.32 (m, 5 H); IR 3060 (w), 3030 (w), 2820 (w), 1720 (st br), 1500 (st br) cm^{-1}; MS m/e (%) 300 (M$^+$, 5), 273 (2), 257 (10), 237 (15), 43 (100); HRMS calcd for $C_{15}H_9F_5O$ 300.057347, found 300.0570.

2-Methyl-3-(pentafluorophenyl)-3-phenyl-1-propene (21). Diiodomethane, 6.0 mL (20.1 g, 75 mmol), was added to a vigorously stirred suspension of 8.8 g (135 mmol) of zinc dust in 90 mL of THF under argon. After stirring at 25 °C for 35 min, the mixture was cooled to −5 °C (ice/salt), and a solution of 2.8 g (1.65 mL, 15 mmol) of titanium tetrachloride in 20 mL of dichloromethane was added over 15 min (*CARE*: can be vigorous). The mixture was then stirred at 25 °C for 75 min. 1-Phenyl-1-(perfluorophenyl)-2-propanone, 3.0 g (10 mmol), was added, and the mixture was stirred at 25 °C for 2.5 h. The mixture was diluted with 200 mL of hexane, 200 mL of 30% NaOH was added, and the layers were separated. The aqueous material was extracted with 2 × 100 mL of hexane. The combined extracts and organic layer were concentrated to give a yellow oil, which was diluted with 100 mL of hexane and dried over magnesium sulfate. Filtering this solution through a short column of activated alumina and evaporation of the solvent gave 3.03 g (10 mmol), 100%, of the product as mobile pale yellow oil: ^{1}H NMR 1.81 (s, 3 H), 4.64 (s, 1 H), 5.03 (s, 1 H), 5.11 (s, 1 H), 7.23–7.31 (m, 5 H); ^{13}C NMR 22.0 (CH$_3$), 47.7 (CH), 114.5 (CH$_2$), 126.9 (CH), 128.3 (CH), 128.5 (CH), 138.5 (C), 142.3 (C); ^{19}F NMR −162.3, −156.5, −140.5; IR 3080 (m), 3030 (m), 2770 (m), 2950 (m), 1650 (w), 1520 (st), 1500 (st br), 1120 (st); MS m/e (%) 298 (M$^+$, 70), 283 (100), 269 (30), 257 (20), 237 (40); HRMS calcd for $C_{16}H_{11}F_5$ 298.078082, found 298.07748.

Catalyzed Hydroboration of 2-Methyl-3-(pentafluorophenyl)-3-phenyl-1-propene (21). Syntheses of *syn*-2-Methyl-3-phenyl-3-(perfluorophenyl)-1-propanol (22) and *anti*-2-Methyl-3-(pentafluorophenyl)-3-phenyl-1-propanol (23). A Schlenk tube was charged with 4.9 mg (0.01 mmol) of chloro(1,5-cyclooctadiene)rhodium(I) dimer and 11.0 mg (0.041 mmol) of triphenylphosphine, evacuated, and flushed with argon five times. THF (1.0 mL) was added, and the bright yellow solution was stirred at 25 °C for 5 min. 2-Methyl-1-(pentafluorophenyl)-1-phenyl-2-propene (0.150 g, 0.5 mmol) was added followed by 2 mL of THF; the mixture was cooled in ice, and 0.12 g (1.0 mmol) of catecholborane was added. The mixture was left to stand at 25 °C for 48 h and then cooled in ice; 1.5 mL of EtOH, 1.5 mL of 3 M NaOH, and 1.0 of mL of 30% hydrogen peroxide were added in that order. The mixture was stirred vigorously for 10 h at 25 °C, diluted with 20 mL of 1 M NaOH, and extracted with 3 × 40 mL of ether. The combined ether extracts were dried, and evaporation of the solvents gave the crude product which was purified by flash chromatography, eluting with 10% ethyl acetate in hexane to give 19 mg (0.06 mmol), 12%, of *anti*-2-methyl-3-(pentafluorophenyl)-3-phenyl-1-propanol and 38 mg (0.12 mmol), 24%, of *syn*-2-methyl-3-(pentafluorophenyl)-3-phenyl-1-propanol. HPLC analysis of the crude showed it to be a 2.6:1.0 syn:anti mixture: IR (neat 1:1 mixture of isomers) 3360 (st br), 3100 (w), 3080 (w), 3040 (m), 2960 (st br), 2890 (s), 1655 (st), 1605 (m), 1500 (st br), 1110 (st), 1040 (st), 980 (st br). ***syn*-2-Methyl-3-phenyl-3-(perfluorophenyl)-1-propanol (22)**: TLC R_f 0.17 (10% ethyl acetate in hexane); ^{1}H NMR 1.02 (d, J = 6.7 Hz, 3 H), 1.26 (br s, 1 H), 2.86 (m, 1 H), 3.39 (dd, J = 5.4, 10.7 Hz, 1 H), 3.59 (dd, J = 3.1, 10.7 Hz, 1 H), 4.25 (d, J = 11.9 Hz, 1 H), 7.20–7.41 (m, 5 H); ^{13}C NMR 16.0 (CH/CH$_3$), 36.2 (CH/CH$_3$), 44.1 (CH/CH$_3$), 65.2 (CH$_2$), 127.2 (CH), 127.9 (CH), 128.8 (CH), 140.2 (C); ^{19}F NMR −162.2, −157.2, −141.9; MS m/e (%) 316 (M$^+$, 3), 398 (80), 273 (40), 257 (100), 237 (60); HRMS calcd for $C_{16}H_{13}F_5$ 316.088645, found 316.08856. ***anti*-2-Methyl-3-(pentafluorophenyl)-3-phenyl-1-propanol (23)**: TLC R_f 0.23 (10% ethyl acetate in hexane); ^{1}H NMR 0.99 (d, J = 6.7 Hz, 3 H), 1.30 (s, 1 H), 2.87 (m, 1 H), 3.47 (m, 1 H), 3.65 (m, 1 H), 4.20 (d, J = 11.8 Hz, 1 H), 7.22–7.39 (m, 5 H); ^{13}C NMR 16.1 (CH/CH$_3$), 35.8 (CH/CH$_3$), 44.3 (CH/CH$_3$), 66.0 (CH$_2$), 127.0 (CH), 128.0 (CH), 128.6 (CH); ^{19}F NMR −162.1, −157.3, −141.6; MS m/e (%) 316 (M$^+$, 2), 298 (40), 283 (15), 257 (60), 237 (40–), 31 (100); HRMS calcd for $C_{16}H_{13}F_5$ 316.088645, found 316.08856.

Uncatalyzed Hydroboration of 2-Methyl-3-(pentafluorophenyl)-3-phenyl-1-propene (21). Alternative Synthesis of *syn*-2-Methyl-3-phenyl-3-(perfluorophenyl)-1-propanol (22) and *anti*-2-Methyl-3-(pentafluorophenyl)-3-phenyl-1-propanol (23). A solution of 0.1 g (0.3 mmol) 2-methyl-1-(pentafluorophenyl)-1-phenyl-2-propene in 6 mL of THF was cooled to −78 °C, 2 mL of 0.5 M solution of 9-BN was added, and the mixture was stirred for 5 min. The solution was stored at −25 °C for 72 h. At 0 °C, 1 mL of EtOH, 2.0 mL of 3 M NaOH, and 1.0 mL of 30% hydrogen peroxide were added in that order; the mixture was stirred at 25 °C for 4 h, diluted with 100 mL of ether, washed with 20 mL of 1 M sodium hydroxide and 20 mL of saturated aqueous ammonium chloride, and dried. HPLC analysis of the crude showed the product alcohols to be a 1.0:1.5 syn:anti mixture.

Cyclized Derivative of *anti*-2-Methyl-3-phenyl-3-(perfluorophenyl)-1-propanol (24). A solution of *anti*-2-methyl-3-(pentafluorophenyl)-3-phenyl-1-propanol, 0.260 g (0.8 mmol), in 10 mL of THF was added to a vigorously stirred suspension of 0.08 g of sodium hydride (1.6 mmol of a 50% dispersion in oil) in 2 mL of THF under nitrogen. The mixture was heated to reflux, stirred for 11 h, diluted with 50 mL of ether, and washed with water. The ether solution was dried over magnesium sulfate and concentrated to give a clear oil. Flash chromatography, eluting with 3% ethyl acetate in hexane, gave 0.166 g (0.56 mmol), 70%, of the product as a white crystalline solid: mp 119–120 °C; ^{1}H NMR (C_6D_6) 0.66 (d, J = 7.0 Hz, 3 H), 1.55 (m, 1 H), 3.31 (ddd, J = 0.9, 5.1, 11.0 Hz, 1 H), 3.51 (d, J = 4.2 Hz, 1 H), 3.64 (dd, J = 2.8, 11.0 Hz), 6.77 (m, 2 H), 7.11 (m, 3 H); ^{13}C NMR (C_6D_6) 15.7 (CH/CH$_3$), 34.3 (CH/CH$_3$), 42.0 (CH/CH$_3$), 67.2 (CH$_2$), 126.6 (CH), 127.2 (CH), 128.3 (CH), 143.2 (C); ^{19}F NMR −169.3, −163.9, −159.1, −143.1; IR ($CHBr_3$) 3021 (m), 2966 (m), 2966 (m), 2935 (m), 1655 (m), 1600 (w), 1490 (st, br); MS 296 (M$^+$ 35), 281 (5), 253 (100); HRMS calcd for $C_{16}H_{12}F_4O$ 296.082418, found 296.08250.

X-ray Diffraction Analysis. A clear, colorless crystal of **24** was mounted on the tip of a glass fiber with epoxy cement. Data

were collected on a Rigaku AFC5S single-crystal, automated four-circle diffractometer using Mo Kα radiation. The cell was determined to be C-centered monoclinic following data reduction of the primitive triclinic unit cell, obtained from a least-squares fit of 22 random reflections. Crystal symmetry was confirmed by the Laue symmetry check. Intensity statistics and systematic absences indicated crystalline in the acentric spacegroup *Cc* (no 9), which was confirmed by successful refinement of the structure. The structure was solved with SHELXS86[63] followed by successive least-squares full-matrix difference refinements (TEXSAN v. 2.0)[64] to convergence with $R = 0.063$ and $R_w = 0.068$. The fluorine and oxygen atoms were refined anisotropically to convergence; carbon atoms were refined with isotropic thermal parameters. The hydrogen atoms were included in calculated positions but were not refined. Equivalent reflections were averaged, and the data were corrected for Lp effects and anomalous dispersion. Corrections for decay and absorption were not applied.

(63) Sheldrick, G. M. (1986). *SHELX*. University of Gottingen, Federal Republic of Germany.
(64) Molecular Structure Coorporatiion. TEXASN (2.0), Program for Crystal Structure Determination and Refinement; The Woodlands, TX. Cromer, D. T.; Waber, J. T. *International Tables for X-Ray Crystallography*; Kynoch Press: Birmingham, 1974; Vol. IV, p 71 (scattering factors), p 148 (anamalous dispersion) (current distributor: Kluwer Academic Publishers, Dordrecht).

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Supplementary Material Available: An ORTEP diagram and tables of crystallographic data collection, atomic coordinates, and anisotropic thermal parameters are available (4 pages). Ordering information is given on any current masthead page.

Manipulation of Substrate-Controlled Diastereoselectivities in Hydroborations in Acyclic Allylamine Derivatives

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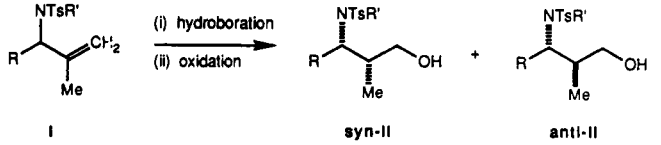
Racemic, and optically active, 2-methyl-3-(*N*-tosylamino)alkenes I were prepared and subjected to both catalyzed and uncatalyzed hydroborations. Data obtained for the catalyzed hydroborations of these allylamine derivatives are consistent with the theory of secondary orbital interactions in transition metal mediated processes presented in the preceding paper. Surprisingly, diastereoselectivities for conventional (uncatalyzed) hydroborations of the same substrates can be extremely sensitive to the borane used; anti products result when borane–tetrahydrofuran complex is reacted with substrates I (R′ = Bn), while with 9-BBN (9-borabicyclo[3.3.1]nonane) these reactions are syn selective. Some of these results are contrary to expectations based upon experimental and theoretical data in the current literature for hydroboration of allylic alcohols. Methodology described in this paper facilitates syntheses of amine alcohols II with extremely high syn and anti selectivities.

The previous paper illustrates that catalyzed and uncatalyzed hydroborations of chiral allylic alcohol derivatives tend to be syn and anti selective, respectively, and gives a model describing secondary orbital effects to account for this difference. As a test of this rationale we decided to explore catalyzed and uncatalyzed hydroborations of allylic *amines* I. Consequently, this paper describes routes to racemic and optically active alkenes I and hydroborations of these. The objectives of this study were (i) to explore "stereocomplementary" behavior which could be exploited in organic syntheses and (ii) to use arguments based on reactive conformations to develop highly diastereoselective syntheses of products II via logical manipulation of the N-protecting groups of substrates I.



I syn-II anti-II

Hydroborations of α-chiral allylic amines have considerable potential in asymmetric syntheses but, to the best of our knowledge, they have been almost[1] totally neglected. Lack of activity in this area is unfortunate because it encompasses preparations of chiral amino alcohols, valuable starting materials for syntheses of new amino acid analogues, β-lactams, and other substances of pharmaceutical interest.[2-8]

Syntheses of Allylamine Derivatives 2–15. This study focuses upon *N*-tosyl-protected allylamine derivatives, principally because absolute stereochemistry at enolizable centers can be preserved when proximal TsN*H* protons are removed preferentially.[9-11] However, there are other reasons for using this particular N-protecting group. Firstly, nitrogen nucleophilicity of tosylamides is poor, hence this functionality has low affinity for com-

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