(*p*-methoxycinnamoyl)tetrazole,[7] is similar to that of tetracinnamate **4**; *30-OH must thus be anti to adjacent 31-OH*. It follows that amino tetrol **1** is 31*R*,32*R*,33*S*,34*S*, and amino pentol **2** is 30*R*,31*R*,32*R*,33*S*,34*S*.

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Amide-Directed, Iridium-Catalyzed Hydroboration of Olefins: Documentation of Regio- and Stereochemical Control in Cyclic and Acyclic Systems

David A. Evans* and Gregory C. Fu[1]

Department of Chemistry, Harvard University
Cambridge, Massachusetts 02138
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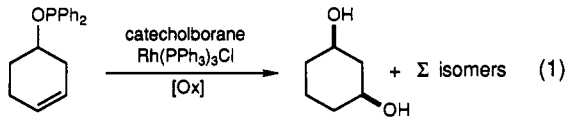
A "directed reaction" is a process in which a functional group transiently binds a reagent and delivers it to a second functionality within the molecule. High levels of regio- and stereocontrol often result from the multiple contact points that are established between the reacting partners in the transition structure. Recent examples of directed hydrogenation and ketone reduction serve to illustrate this point.[2]

Although a number of reactions have been shown to be directable, no general approach to effecting a directed olefin hydroboration with BH_3 or alkylboranes has been reported.[3,4] The lack of success in this area may well arise from constraints inherent to the uncatalyzed hydroboration process.[5] The discovery of a rhodium-catalyzed variant by Mannig and Noth[6] revived the prospects for the development of a directable olefin hydroboration. Indeed, we reported in 1988 that phospinites are capable of delivering the rhodium-mediated reaction (eq 1);[7] however, because *stoichiometric* quantities of $Rh(PPh_3)_3Cl$ are required, this method fell short of accomplishing our goal of developing a *catalytic* directed hydroboration. In this communication we report that amides effectively direct the $[Ir(cod)(PCy_3)(py)]PF_6$[2c]-catalyzed hydroboration of olefins with catecholborane (CB), an observation that represents a fulfillment of our original objective.



diastereoselection 98 : 2 (82%)

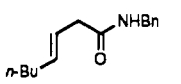
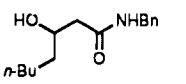
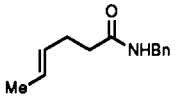
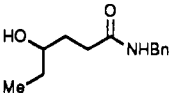
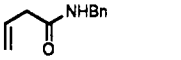
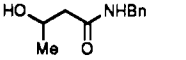
A number of functional groups known to direct metal-catalyzed olefin hydrogenation were screened for participation in the analogous hydroboration process with catecholborane.[8] From this survey, amides were found to be quite effective at actively participating in the hydroboration process.[9] For example, $[Ir(cod)(PCy_3)(py)]PF_6$-catalyzed hydroboration[7] of pyrrolidinyl amide **1** (2 equiv of CB, 5% catalyst, 11 h, 20 °C, $ClCH_2CH_2Cl$) affords the syn-1,3 hydroxy amide (eq 2) with good control of both regio- and stereoselectivity (95:5).[10,11] Competitive reduction of the tertiary amide moiety, the origin of the modest yield observed in this reaction, is readily avoided through the use of more reduction resistant secondary amides (**2a**; 5 equiv of CB, 5% catalyst, 10 h, 20 °C, $ClCH_2CH_2Cl$) as the directing group (eq 3).

Table I. Solvent Effect on the Stereoselectivity of the Amide-Directed Hydroboration (Eq 2)

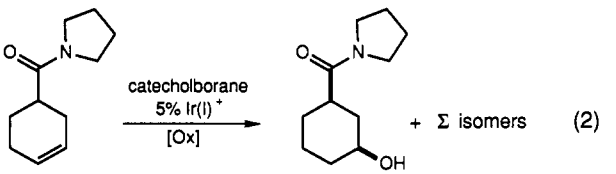
solvent	syn-1,3: Σ(other 3 isomers)[a]
THF	45:55
ether	52:48
$ClCH_2CH_2Cl$	95:5

[a] Ratios determined by GLC on derived acetates.

Table II. Amide-Directed, Catalyzed Hydroboration: Acyclic Cases[15]

entry	substrate	product	selectivity[a] (% yield)
1			>99:1 (73)
2			99:1 (78)
3			1.2:1 (78)

[a] Ratio of proximal:distal hydroxylation, as determined by GLC.



2a, R = CONHBn *diastereoselection 91 : 9 (77%)*
2b, R = COOMe
2c, R = OSi(*tert*-Bu)Me_2

The following observations support the assertion that these reactions are amide-directed:

Stereoselectivity. The catalyzed hydroboration of a variety of other 4-substituted cyclohexenes, which include derivatives such as **2b** or **2c**, furnish an essentially statistical mixture of the four isomeric reaction products. Predominant formation of the syn-1,3 isomer (eqs 2 and 3) is consistent with the expectation of a directed reaction.[12]

(1) National Science Foundation Predoctoral Fellow.
(2) Directed hydrogenation: (a) Brown, J. M. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 190-203. (b) Evans, D. A.; Morrissey, M. M. *J. Am. Chem. Soc.* **1984**, *106*, 3866-3868. (c) Crabtree, R. H.; Davis, M. W. *J. Org. Chem.* **1986**, *51*, 2655-2661. Directed ketone reduction: (d) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560-3578. (e) Evans, D. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1990**, *112*, 6447-6449.
(3) Several workers have proposed reaction pathways involving the delivery of a boron hydride in order to explain anomalous regio- and stereoselectivities observed in uncatalyzed olefin hydroboration reactions. For example, see: (a) Suzuki, K.; Miyazawa, M.; Shimazaki, M.; Tsuchihashi, G.-i. *Tetrahedron* **1988**, *44*, 4061-4072. (b) Welch, M. C.; Bryson, T. A. *Tetrahedron Lett.* **1989**, *30*, 523-526.
(4) (a) For a report of an unsuccessful attempt to achieve a hydroxyl-directed hydroboration, see: Smith, A. B., III; Yokoyama, Y.; Huryn, D. M.; Dunlap, N. K. *Tetrahedron Lett.* **1987**, *28*, 3659-3662. (b) For a discussion of the likelihood of directivity in the hydroboration of a homoallylic alcohol with borane, see: Heathcock, C. H.; Jarvi, E. T.; Rosen, T. *Tetrahedron Lett.* **1984**, *25*, 243-246.
(5) For a discussion of the mechanism of the uncatalyzed hydroboration reaction, see: Wang, X.; Li, Y.; Wu, Y.-D.; Paddon-Row, M. N.; Rondan, N. G.; Houk, K. N. *J. Org. Chem.* **1990**, *55*, 2601-2609.
(6) Mannig, D.; Noth, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 878-879.
(7) Evans, D. A.; Fu, G. C.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1988**, *110*, 6917-6918.
(8) For a review of directed hydrogenation reactions, see ref 2a.
(9) Schultz, A. G.; McCloskey, P. J. *J. Org. Chem.* **1985**, *50*, 5905-5907.
(10) The cited selectivities refer to the ratio of the illustrated isomer to the sum of all other isomers. Product analyses were carried out by capillary GLC on the derived acetates.
(11) We have also examined the utility of $Rh(PPh_3)_3Cl$ and $[Rh(nbd)(diphos-4)]BF_4$ (nbd = norbornadienyl) as catalysts for amide-directed hydroboration. In some cases, use of these complexes affords selectivity comparable to that observed with $[Ir(cod)(PCy_3)(py)]PF_6$. In general, however, significantly lower selectivities are obtained.
(12) For example, see: Tamao, K.; Nakajima, T.; Sumiya, R.; Arai, H.; Higuchi, N.; Ito, Y. *J. Am. Chem. Soc.* **1986**, *108*, 6090-6093.

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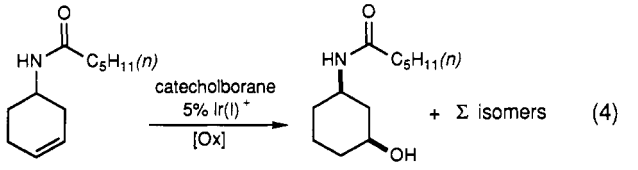
Enhanced Reactivity. In a competition experiment, *N*-benzylcarboxamide **2a** is over 1 order of magnitude more reactive toward iridium-catalyzed hydroboration than is silyl ether **2c**. Given the remoteness of the substituent from the olefin, a steric or an electronic effect is unlikely to be the origin of this disparity in relative reaction rates.[13]

Solvent Effect on Stereoselectivity. The data in Table I for the hydroboration of amide **1** reveal an inverse relationship between the Lewis basicity of the solvent and the level of diastereoselectivity observed. This trend may readily be rationalized if the amide is delivering the metal through Lewis acid–base complexation: When the solvent is better able to compete with the amide for complexation to the metal, the directed pathway becomes less favorable, and an erosion in stereoselectivity results.

Additional examples serve to illustrate the generality of amide delivery of the iridium-catalyzed hydroboration reaction. For example, we have found that amides derived from cyclic homoallylic amines such as **3** can also direct the process (eq 4).[14]



3 *diastereoselection 88 : 12 (69%)*

The directing ability of the amide moiety is also evident in acyclic systems (Table II). Iridium-catalyzed hydroboration of the illustrated β,γ-unsaturated amide (entry 1) affords the β-hydroxy amide with >99:1 selectivity, while the analogous reaction of a homologue (entry 2) is only slightly less regioselective (99:1). In fact, the amide directing group is capable of turning over the normal regiochemical preference of the iridium-catalyzed hydroboration of a terminal olefin. Whereas 1-hexene undergoes hydroboration with 98:2 selectivity favoring formation of the primary alcohol, reaction of the 3-butenamide (entry 3) affords the *secondary* alcohol as the major product (1.2:1).[15]

In conclusion, this study demonstrates that amides effectively direct the $[Ir(cod)(PCy_3)(py)]PF_6$-catalyzed hydroboration of olefins with catecholborane, producing hydroxy amides with high levels of regio- and stereochemical control; this reaction represents the first application of iridium-catalyzed hydroboration to organic synthesis. In contrast to the rhodium-mediated, phosphinite-directed process uncovered earlier, the amide-directed reaction proceeds in the presence of a *catalytic* quantity of the metal complex. Further studies of diastereo- and enantioselective amide-directed hydroboration are planned.

Acknowledgment. Support has been provided by the National Institutes of Health. The NIH BRS Shared Instrumentation Grant Program 1 S10 RR01748-01A1 is acknowledged for providing NMR facilities.

Supplementary Material Available: Selected experimental procedures, as well as spectral and analytical data for all reaction products (4 pages). Ordering information is given on any current masthead page.

(13) We have also shown separately that, in contrast to the hydroxyl-directed, $[Ir(cod)(PCy_3)(py)]PF_6$-catalyzed olefin hydrogenation reaction (ref 2c), the amide-directed, $[Ir(cod)(PCy_3)(py)]PF_6$-catalyzed hydroboration process is *not* ligand-decelerated.

(14) Yield based on recovered starting material.

(15) Typical procedure: Catecholborane (300 mg, 2.50 mmol) was added to a mixture of **2a** (108 mg, 0.50 mmol) and $[Ir(cod)(PCy_3)(py)]PF_6$ (20.1 mg, 0.025 mmol) in 2.0 mL of $ClCH_2CH_2Cl$. The resulting homogeneous, pale yellow solution was stirred at 20 °C for 10 h and then subjected to an oxidative workup [1.0 mL of EtOH:THF (1:1), 1.0 mL of pH 7.00 buffer (0.05 M potassium phosphate monobasic sodium hydroxide), and 1.0 mL of 30% H_2O_2] for 12 h at 20 °C. The oxidized mixture was isolated by extraction, and then the unpurified reaction product was acetylated in order to ease diastereomer analysis. GLC analysis of an aliquot revealed a 91:9 [syn-1,3:Σ(other isomers)] mixture of acetates. The acetates were purified by flash chromatography, which afforded 106 mg (77%) of the acetylated hydroxy amides.

Hyperbranched Poly(siloxysilanes)

Lon J. Mathias* and Terrell W. Carothers

Department of Polymer Science
University of Southern Mississippi
Hattiesburg, Mississippi 39406-0076

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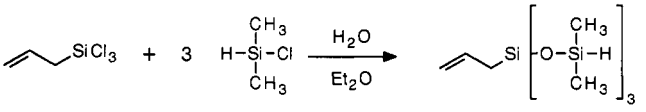
Starburst dendrimers, polymers, and arborols were synthesized by Tomalia et al.[1,2] and Newkome et al.,[3] respectively. These materials have precisely determined branch contents and branch lengths, but synthetic requirements are demanding and time-consuming. An alternative is to use multifunctional step-growth monomers, AB_n, where n determines the number of branches per repeat unit.[4] Two recent reports describe the synthesis of hyperbranched polyphenylenes[5] and polyamines.[6] The present report describes the use of hydrosilation to obtain highly branched polymers containing silane and siloxane groups. During the lengthy evaluation of our manuscript, a communication appeared on materials structurally very similar.[7]

The monomer chosen for initial study contains an allyl moiety and three Si–H groups. Monomer synthesis involved addition of allyltrichlorosilane to 3 equiv of dimethylchlorosilane in a mixture of ether and water. Yields of **1** were surprisingly good (>50%, >98% pure after distillation) in view of possible side reactions. Spectral and physical data confirm the structure.



1

Polymerization of **1** occurred in a 1:1 mixture of acetonitrile and ether under N_2 using hydrogen hexachloroplatinate(IV) hydrate (Aldrich). Stirring was continued at 52 °C for 8 h. Polymer isolation by addition of water gave **2** in the organic layer and catalyst in the aqueous phase. The FTIR spectrum of **2** shows essentially complete disappearance of the vinyl peak (1635 cm^{-1}) and reduction of the Si–H peak (2200 cm^{-1}).

The ^1H NMR spectrum ($CDCl_3$) of **1** showed peaks for allyl at δ 1.5 (allyl CH_2), δ 4.9 (vinyl β-CH_2), and δ 5.7 (vinyl α-CH). The Si–H peak appeared at δ 4.7 as a multiplet (coupling to two CH_3's). **2** showed almost no vinyl peaks. Integration of Si–H vs repeat unit peaks indicated chain extension to the third or fourth generation (average MW 11 000–35 000). Size-exclusion chromatography (THF) gave a single, narrow peak corresponding to a polystyrene standard of 19 000. Formation of this polymer was rapid, and addition of more catalyst did not increase its molecular weight, suggesting sterically inhibited chain extension. Molecular simulations of polyamide starburst dendrimers illustrate such outer-surface steric crowding.[8] Clearly, facile formation of polymer is possible with this system, although the absolute molecular weight, molecular weight distribution, and uniformity of branching have not yet been determined.

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