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# Trifluoromethyl-Substituted Indenyl Rhodium and Iridium Complexes Are Highly Selective Catalysts for Directed Hydroboration Reactions

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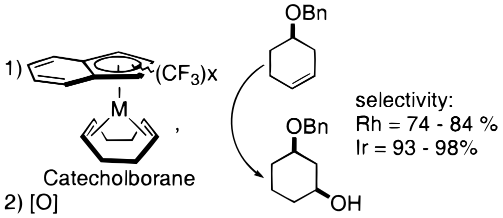
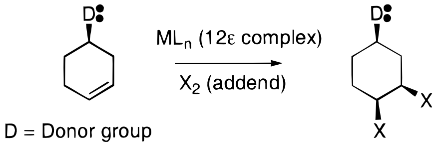
## ABSTRACT



**Rhodium and iridium catalysts containing trifluoromethyl-substituted indenyl ligands (Ind′MCod, Ind′ = $C_9H_7$, (1-$CF_3$)$C_9H_6$, (2-$CF_3$)$C_9H_6$, (1,3-$CF_3$)$_2C_9H_5$) have been developed for the directed hydroboration of 4-(benzyloxy)cyclohexene to *cis*-3-(benzyloxy)cyclohexanol. Compared to unsubstituted complexes, trifluoromethyl substitution yields a 3–10% increase in selectivity which is attributed to the strong electron-withdrawing effect of the trifluoromethyl group. Rhodium complexes give selectivities of 74–84%, and iridium complexes give high levels of selectivity (93–98%).**

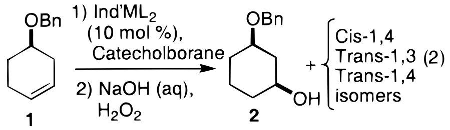
Directed reactions are an important class of stereoselective, transition-metal-mediated processes.[1] In these reactions, donor groups (D) direct reactions to occur on the same face of the substrate as the donor group (eq 1).[2] A requirement of the transition metal is that it must achieve the requisite degree of coordinative unsaturation to facilitate the directed reaction. Crabtree proposed that the metal must achieve a $12\epsilon$ count or less in order to simultaneously accommodate the directing group, the addend ($X_2$), and the target functional group of the substrate which is often an olefin (eq 1).[3]



(1)

In 1998, Garrett and Fu[2] demonstrated that the indenyl ligand could enable a transition metal to obtain the required degree of coordinative unsaturation by slipping from a $6\epsilon$ donor ($\eta^5$-Ind) to a $4\epsilon$ donor ($\eta^3$-Ind).[15] The indenyl ligand was chosen because of its propensity to undergo coordinative isomerization from $\eta^5$- to $\eta^3$-coordination.[4] This process, also known as ring slippage, allows the metal to accommodate the $2\epsilon$ donor ligand (D) and dramatically increases rates of ligand substitution reactions.[5]

With IndRh($C_2H_4$)$_2$, Fu and Garrett obtained 75% selectivity for the directed hydroboration of 4-(benzyloxy)cyclohexene (**1**) to *cis*-(3-benzyloxy)cyclohexanol (**2**) (eq 2).[2] We chose to further examine this reaction using rhodium and iridium complexes containing trifluoromethyl-substituted indenyl ligands. The syntheses of indenes **3**−**5** are previously reported.[6] The corresponding rhodium and iridium complexes



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[1] Review: Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307−1370.
[2] Garrett, C. E.; Fu. G. C. *J. Org. Chem.* **1998**, *63*, 1370−1371.

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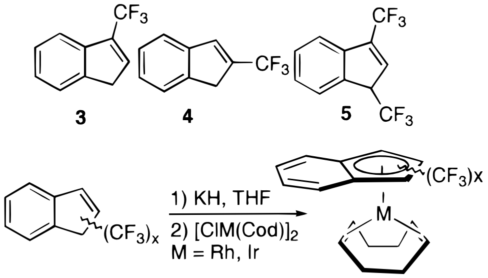
are prepared by deprotonation of the indene followed by reaction with $[ClM(Cod)]_2$, M = Rh or Ir (Scheme 1).[7]

**Scheme 1.** Trifluoromethyl-Substituted Indenes and Catalyst Preparation[6,7]



Our previous work examined the effect of trifluoromethyl-substituted indenyl ligands in the rhodium-catalyzed hydroboration of styrene.[8] In that study, there was no difference in yield or selectivity between the unsubstituted and trifluoromethyl-substituted indenyl catalysts, suggesting that the indenyl ligand was being removed from the catalyst. The lability of anionic olefin ligands (e.g., $\eta^3$-allyl) under conditions of hydroboration is well known.[9] However, the study by Garrett and Fu[2] indicates that the indenyl ligand remains intact during the course of the directed hydroboration reaction. Moreover, they found that electron-donating methyl groups decrease selectivity compared to the unsubstituted ligand. We reasoned that if indeed the indenyl ligand remained intact, then electron-withdrawing groups will increase selectivity. However, indenyl complexes with electron-withdrawing substituents have not been widely explored.[10] The catalysts that we have chosen contain one or two trifluoromethyl groups attached to various positions on the indenyl ring as shown in Scheme 1.

The proposed mechanism for the directed hydroboration reaction involves initial loss of the ethylene ligands to form a 14$\epsilon$ intermediate.[2] Since the catalysts we have developed contain the 1,5-cyclooctadiene ligand (Cod) instead of bis-ethylene, we first compared the selectivity and yield of IndRh(Cod) to that of $IndRh(C_2H_4)_2$.[11] The results indicate that these are equivalent catalysts (Table 1).

After confirming that the Cod ligand does not affect reactivity and product ratios, we studied a series of trifluoromethyl-substituted Ind′Rh(Cod) catalysts. The first complex, $(1\text{-}CF_3Ind)Rh(Cod)$, showed a 7% increase in selectivity to 81% for the *cis*-1,3 isomer (**2**). The run was repeated in triplicate, and the selectivity was remarkably reproducible with a variation of ±1%. With the trifluoromethyl group at the 2-position of the indenyl ligand, $(2\text{-}CF_3Ind)Rh(Cod)$, there was no change in selectivity (81%). However, the catalyst with two trifluoromethyl groups, $(1,3\text{-}(CF_3)_2Ind)Rh(Cod)$, resulted in a further increase in selectivity to 84% for the *cis*-1,3 isomer.

**Table 1.** Selectivity and Yield of Rhodium-Catalyzed Directed Hydroborations

| catalyst Ind′RhL$_2$ | *cis*-1,3[a] | *cis*-1,4[a] | *trans*-1,3[a] | *trans*-1,4[a] | yield,[c] % |
|---|---|---|---|---|---|
| $IndRh(C_2H_4)_2$ | 73 (75)[b] | 10 (7) | 11 (8) | 7 (11) | 71 (78) |
| IndRh(Cod) | 74 | 11 | 9 | 6 | 70 |
| $(1\text{-}CF_3Ind)Rh(Cod)$ | 81 | 5 | 10 | 4 | 59 |
| $(2\text{-}CF_3Ind)Rh(Cod)$ | 81 | 6 | 9 | 4 | 58 |
| $(1,3\text{-}(CF_3)_2\text{-}Ind)Rh(Cod)$ | 84 | 3 | 8 | 5 | 59 |

[a] Selectivity determined by HPLC with authentic standards. [b] Previously reported selectivities and yield, ref 2. [c] Isolated yield of the four isomers.

Although the selectivities are markedly increased with the trifluoromethyl-substituted catalysts, the yields of the reactions are ~10% lower than the unsubstituted catalysts. Furthermore, the reactions (substituted or unsubstituted catalysts) are extremely air sensitive and failure to exclude air significantly reduces selectivity or completely inhibits the reaction. In agreement with Garrett and Fu, we find that best results are obtained with freshly prepared and distilled catecholborane.[12]

Previous studies have shown that Crabtree's iridium complex, $[Ir(cod)(PCy_3)(py)]PF_6$, is a more selective catalyst than $[Rh(nbd)(dppb)]BF_4$ in amide-directed hydroborations.[13] Thus, it seemed likely that a switch from rhodium to iridium in our system would also result in an increase in selectivity. This insight proved to be valuable as selectivity for the *cis*-1,3 isomer increased to practical levels (93−98%) with the iridium-based catalysts (Table 2). For example, a 19% increase in selectivity is observed on going from the unsubstituted IndRh(Cod) (74%) complex to IndIr(Cod) (93%). Furthermore, the diastereoselective trend of increasing

**Table 2.** Yield and Selectivity of Iridium-Catalyzed Directed Hydroborations

| catalyst Ind′Ir(Cod) | *cis*-1,3[a] | *cis*-1,4[a] | *trans*-1,3[a] | *trans*-1,4[a] | yield,[b] % |
|---|---|---|---|---|---|
| IndIr(Cod) | 93 | <1 | 5 | 2 | 72 |
| $(1\text{-}CF_3Ind)Ir(Cod)$ | 96 | <1 | 2 | 2 | 60 |
| $(2\text{-}CF_3Ind)Ir(Cod)$ | 96 | 2 | 2 | <1 | 62 |
| $(1,3\text{-}(CF_3)_2\text{-}Ind)Ir(Cod)$ | 98 | 2 | <1 | <1 | 60 |

[a] Selectivity determined by HPLC with authentic standards. [b] Isolated yield of the four isomers.

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selectivity with increasing trifluoromethyl substitution seen with the rhodium complexes is also observed with iridium. Using mono-trifluoromethyl indenyl iridium complexes increases the selectivity to 96%. Furthermore, using the (1,3-$(CF_3)_2$Ind)Ir(Cod) complex yields a catalyst that generates *cis*-(3-benzyloxy)cyclohexanol (**2**) in 98% selectivity.

Compared to unsubstituted systems, catalysts with one trifluoromethyl group give a 3−7% increase in selectivity and an additional 2−3% increase is obtained with catalysts containing two trifluoromethyl groups. This is attributed to the electron-withdrawing effect of the trifluoromethyl group which enhances the ability of the catalysts to accommodate the donor group (OBn). However, it is interesting to consider whether the selectivity is determined by the inherent ability of the indenyl ligand to ring slip or the enhanced electrophilicity of the transition-metal center. In all examples, the trifluoromethyl substituents are located on the allylic portion of the indenyl ligand. Since this is also the anionic fragment of the ligand, the electron-withdrawing trifluoromethyl substituent may stabilize this fragment. This should increase the ability of the indenyl ligand to slip from $\eta^5$- to $\eta^3$-coordination. It is also well known that trifluoromethyl substituents in cyclopentadienyl complexes increase the electrophilicity of the metal center;[1414−15] this is also most certainly true for indenyl complexes. The more electrophilic metal center will enhance the coordination of the OBn donor group. Thus, it is likely that both effects work in combination to accommodate the donor ligand and enhance its directing influence.

The results of this study supports Garrett and Fu's theory that coordinative isomerism of the indenyl ligand, i.e., ring slippage, provides the necessary coordinative unsaturation to facilitate a directed reaction. However, we also show that selectivity is enhanced when electron-withdrawing groups are present on the indenyl ligand. Furthermore, switching from rhodium- to iridium-based systems provides a series of catalysts that give high levels (93−98%) of selectivity for the directed hydroboration reaction of 4-(benzyloxy)-cyclohexene. We are currently exploring the scope of this reaction toward a wider array of substrates and completing an extensive X-ray crystallographic study[7b] of the structures of the rhodium and iridium catalysts used in this study.

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**Supporting Information Available:** General experimental conditions, preparation of catalysts, and general catalytic procedure sections. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) (a) **General experimental procedure:** Manipulations for the hydroboration procedure were performed under an argon atmosphere. **Hydroboration:** a solution of 4-(benzyloxy)cyclohexene[11b,c] (100 mg, 0.53 mmol) in anhydrous hexane (1 mL) was added by syringe to a solution of IndRh(Cod) (17 mg, 0.053 mmol) in anhydrous hexane (4 mL). The light yellow solution was cooled in an ice bath, and catecholborane (0.150 mL, 1.38 mmol) was added to give a pale yellow solution. The reaction mixture was allowed to warm to room temperature and stirred for 24 h. **Oxidation:** the reaction mixture was then cooled in an ice bath and MeOH (2 mL), NaOH (3 N, 2 mL), and 30% $H_2O_2$ (2 mL) were added. The mixture was stirred, with slow warming to room temperature, for 1 h. The reaction mixture was extracted with ether, dried over $MgSO_4$ (anhydrous), and concentrated. The selectivity was determined by HPLC analysis with a reverse phase column (Waters Nova-Pak C-18, 3.9 × 150 mm) using a solvent gradient of 10% acetonitrile/water to 100% acetonitrile over a 20 min period. See Supporting Information in ref 2 for preparation of authentic standards. (b) Godek, C. J.; Moir, R. Y.; Purves, C. B. *Can J. Chem.* **1951**, *29*, 946, (c) Schulz, J.; Gani, D.; *J. Chem. Soc., Perkins Trans. 1* **1997**, 657−670.

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(15) Abbreviations: Bn = benzyl, Cod = 1,5-cyclooctadiene, Cy = cyclohexyl, dppb = 1,4-bis(diphenylphosphino)butane, Ind = indenyl ligand ($C_9H_7$), Ind′ = substituted indenyl ligand, nbd = norbornadiene, py = pyridine.