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Catalytic, Highly Enantio- and Diastereoselective Pinacol Coupling Reaction with a New Tethered Bis(8-quinolinolato) Ligand

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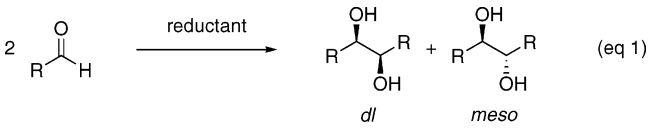
Chiral 1,2-diols are structural motifs often found in various important natural products[1] and have also proven valuable as chiral ligands[2] and auxiliaries[3] in stereoselective organic syntheses. This class of diols has been successfully prepared in enantioenriched forms by resolution of racemic diols,[4] by Sharpless asymmetric dihydroxylation of alkenes,[5] and by asymmetric transfer hydrogenation of 1,2-diketones.[6] Arguably, the most direct method to prepare 1,2-diols is a reductive coupling of simple aldehydes (eq 1).[7] However, the identification of a catalytic asymmetric pinacol coupling reaction has remained a challenge for organic chemistry since not only enantioselectivity but also diastereoselectivity (*dl* vs *meso*) needs to be controlled in a single bond-forming event. High stereoselectivity in pinacol coupling reaction has remained elusive even through stoichiometric protocols.[8] To date, efforts toward this goal have focused on the use of chiral low-valent titanium catalysts.[9−11] Described herein are the development of a new chiral tethered bis(8-quinolinolato) (TBOx)[12] chromium catalyst and its application to the highly enantio- and diastereoselective pinacol coupling reaction of aromatic aldehydes, as well as the first example of an aliphatic aldehyde.

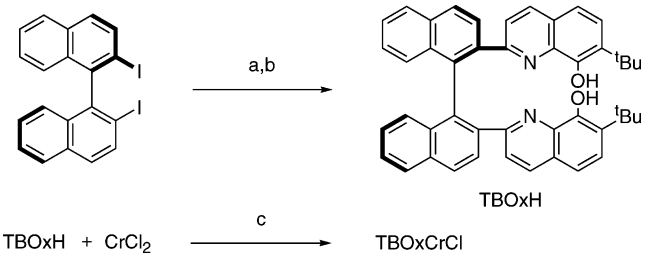


(eq 1)

Simple chromium(II) salts such as $CrCl_2$ and $Cr(ClO_4)_2$ have been reported to promote radical-mediated pinacolic coupling reaction either as a stoichiometric reagent[13] or as a catalyst[14] in the presence of a stoichiometric co-reductant. Fürstner et al. found that the reducing ability of Cp_2Cr toward aromatic aldehydes exceeded that of $CrCl_2$ during the course of his study on chromium-catalyzed Nozaki−Hiyama−Kishi (NHK) reaction.[15] The observed difference between the two was attributed to a Cp ligand that is more electron-rich than a chloride ligand. An electron-rich Cr(II) complex would, therefore, be an attractive candidate as a catalyst for the pinacol coupling reaction. Given the low flexibility for structure modification of chiral Cp-based ligands, our attention was eventually turned to 8-quinolinol as a metal template. The development of an achiral template into an asymmetric chiral ligand was successfully achieved in two steps from 2,2′-diiodo-1,1′-binaphthyl[16] and 7-*tert*-butyl-8-methoxy-quinoline. Its Cr(III) complex was synthesized according to the literature[17] (Scheme 1). To the best of our knowledge, however, no optically active chiral chromium complexes have been studied as a catalyst for pinacol coupling reaction.

In catalytic pinacol coupling reactions, the role of chlorosilane is generally explained as cleaving the metal−oxygen bond of a putative pinacol formed to recycle a catalyst.[10,15a,b] However, interestingly, TESCl provided better stereoselectivities than TMSCl in our system (vide infra).[18] Thus, the precatalyst

Scheme 1. Syntheses of TBOxH and TBOxCrCl[a]



[a] Reaction conditions: (a) ^{t}BuLi, 7-*tert*-butyl-8-methoxy-quinoline, THF, −70 °C, followed by oxidation with tetrachloro-1,2-benzoquinone, 76%. (b) BBr_3, CH_2Cl_2, 95%. (c) THF, reflux, followed by air oxidation, 99%.

Table 1. Reactions of Various Aromatic Aldehydes

entry	Ar	time (h)	yield (%)	*dl*:*meso*	ee (%)
1	Ph	10	94	98:2	97
2	*o*-MePh	18	93	98:2	98
3	*p*-MePh	12	93	97:3	97
4	*m*-MeOPh	12	92	98:2	97
5	*p*-BrPh	10	91	97:3	98
6	*p*-ClPh	9	94	97:3	98
7	*p*-CF_3Ph	20	89	92:8	95
8	1-naph	14	92	96:4	98
9	2-naph	14	88	97:3	95

(TBOxCr(III)Cl), co-reducing agent (Mn), the product scavenger (TESCl), and aldehyde were mixed in CH_3CN under an atmosphere of Ar at room temperature. Significantly, the reaction is effectively catalyzed with 3 mol % of the catalyst, which represents the lowest catalyst/substrate ratio for an asymmetric catalytic pinacol coupling reaction.[11a] The isolated crude silyl ethers were treated with aqueous HCl in THF to afford diols in high yields and excellent enantio- and diastereoselectivities (Table 1).

The present catalyst system proved to be quite insensitive to changes in steric effect (entries 2 and 8 in comparison to 1) and electron withdrawing substituents on the aromatic ring such as Br, Cl, and CF_3 (entries 5, 6, and 7), which significantly lowered enantioselectivities in all cases of the previously reported catalytic pinacol coupling reactions.[11d−f]

The synthesis of pinacols from aliphatic aldehydes requires the use of a more efficient redox system than does the corresponding reductive coupling of aromatic systems.[7b,11f,19] To our surprise, the scope of the present method was found not to be limited to aromatic aldehyde derivatives, as cyclohexanecarboxaldehyde underwent pinacolization (44% yield, *dl*:*meso* = 93:7, 84% ee). This represents

10.1021/ja045430u CCC: $27.50

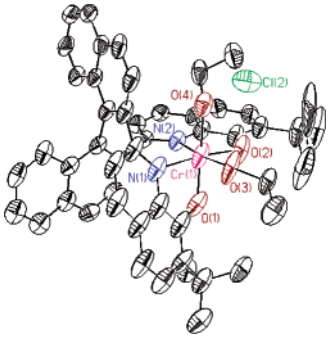
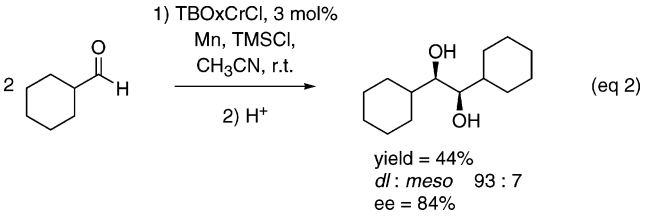


Figure 1. X-ray crystal structure of $[TBOx(EtOH)_2Cr]Cl$.

the first example of the asymmetric catalysis of an aliphatic pinacol coupling reaction (eq 2).



TBOxCrCl may have a total of three geometric isomers,[20] given that it adopts octahedral coordination. The X-ray structure of *rac*-TBOxCrCl revealed that the ligand is bound to a chromium center in a *cis*-β configuration (Figure 1). A crystal structure of *cis*-β configured TBOxCrCl provided valuable information for future mechanistic analysis of the present pinacol reaction.

In summary, a new class of chiral ligand, TBOx, was developed, and the X-ray crystal structure of its chromium complex was determined. TBOxCrCl was shown to efficiently catalyze the asymmetric pinacol coupling reactions of both aromatic and aliphatic aldehydes. Studies are currently underway to elucidate the mechanism and scope of this pinacol coupling reaction. Furthermore, the applications of TBOx in other asymmetric catalysis will be reported in due course.

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Supporting Information Available: Experimental procedures, spectral data for all new compounds, and crystallographic data. X-ray crystallographic file in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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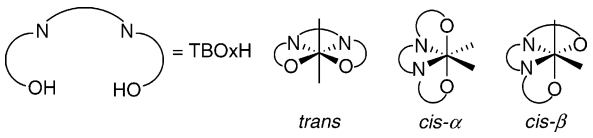

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