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Cationic Co(I)-Intermediates for Hydrofunctionalization Reactions: Regio- and Enantioselective Cobalt-Catalyzed 1,2-Hydroboration of 1,3-Dienes

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Supporting Information

ABSTRACT: Much of the recent work on catalytic hydroboration of alkenes has focused on simple alkenes and styrene derivatives with few examples of reactions of 1,3-dienes, which have been reported to undergo mostly 1,4-additions to give allylic boronates. We find that reduced cobalt catalysts generated from 1,n-*bis*-diphenylphosphinoalkane complexes [Ph_2P-$(CH_2)_n$-PPh_2]CoX_2; n = 1~5) or from (2-oxazolinyl)phenyldiarylphosphine complexes [(G-PHOX)CoX_2] effect selective 1,2-, 1,4-, or 4,3-additions of pinacolborane (HBPin) to a variety of 1,3-dienes depending on the ligands chosen. Conditions have been found to optimize the 1,2-additions. The reactive catalysts can be generated from the cobalt (II)-complexes using trimethylaluminum, methyl aluminoxane or activated zinc in the presence of sodium *tetrakis*[(3,5-trifluoromethyl)phenyl]borate (NaBARF). The complex, (dppp)$CoCl_2$, gives the best results (ratio of 1,2- to 1,4-addition >95:5) for a variety of linear terminal 1,3-dienes and 2-substituted 1,3-dienes. The [(PHOX)CoX_2] (X = Cl, Br) complexes give mostly 1,4-addition with linear unsubstituted 1,3-dienes, but, surprisingly selective 1,2-additions with 2-substituted or 2,3-disubstituted 1,3-dienes. Isolated and fully characterized (X-ray crystallography) Co(I)-complexes, $(dppp)_3Co_2Cl_2$ and [(*S,S*)-BDPP]$_3Co_2Cl_2$, *do not* catalyze the reaction unless activated by a Lewis acid or NaBARF, suggesting a key role for a cationic Co(I) species in the catalytic cycle. Regio- and enantioselective 1,2-hydroborations of 2-substituted 1,3-dienes are best accomplished using a catalyst prepared via activation of a chiral phosphinooxazoline-cobalt(II) complex with zinc and NaBARF. A number of common functional groups, among them, -OBn, -OTBS, -OTs, *N*-phthalimido- groups, are tolerated and er's >95:5 are obtained for several dienes including 1-alkenylcycloalk-1-enes. This operationally simple reaction expands the realm of asymmetric hydroboration to provide direct access to a number of nearly enantiopure homoallylic boronates, which are not readily accessible by current methods. The resulting boronates have been converted into the corresponding alcohols, potassium trifluroroborate salts, *N*-BOC amines and aryl derivatives by *C*-BPin to *C*-aryl transformation.

INTRODUCTION

Regio- and enantioselective hydrofunctionalization of prochiral 1,3-dienes, which are among the most readily available starting materials for organic synthesis, can provide intermediates with multiple latent functionalities for further synthetic elaboration.[1] As one of the most useful hydrofunctionalization reaction, metal-catalyzed vicinal hydroboration of alkenes has a long history.[2,3] However, enantioselective hydroboration of 1,3-dienes to produce chiral intermediates from even the least complex among these substrates, monosubstituted (*E*)-1,3-dienes (**1**, R_1 = H, R_2 = H, R_3 = H, R_4 = alkyl), presents a significant challenge because of the possibility of 1,2- and 1,4- additions leading to chiral and achiral products, and geometrical isomers of the residual double bond in some of the products (Eq 1).[4] Additional substituents, for example, at C_1~C_3 positions further exacerbate this problem and enantioselective hydroborations of di- and trisubstituted 1,3-diene substrates have not been reported. There are several reports of 1,4/4,1-additions of boranes to various acyclic 1,3-dienes.[5] Yet, except for one report of selective additions of catechol borane to (*E*)-penta-1,3-diene (Figure 1 **A**),[6] examples of 1,2-(anti-Markovnikov) hydroborations of substituted 1,3-dienes are limited to two substrates, myrcene[7] and isoprene.[8] While enantioselective Pt-catalyzed 1,2- and 1,4-*diborations* of acyclic 1,3-dienes[1j,9] are known, documented cases of useful levels of regioselectivity and enantioselectivity in 1,2-*hydroboration* in acyclic 1,3-dienes are limited to a publication describing a Cu-catalyzed addition of *bis*-

pinacolborane, that just appeared (Figure 1, **B**, Eq 3),[10] and, our own preliminary disclosure in 2017 (Figure 1 **C**).[11]

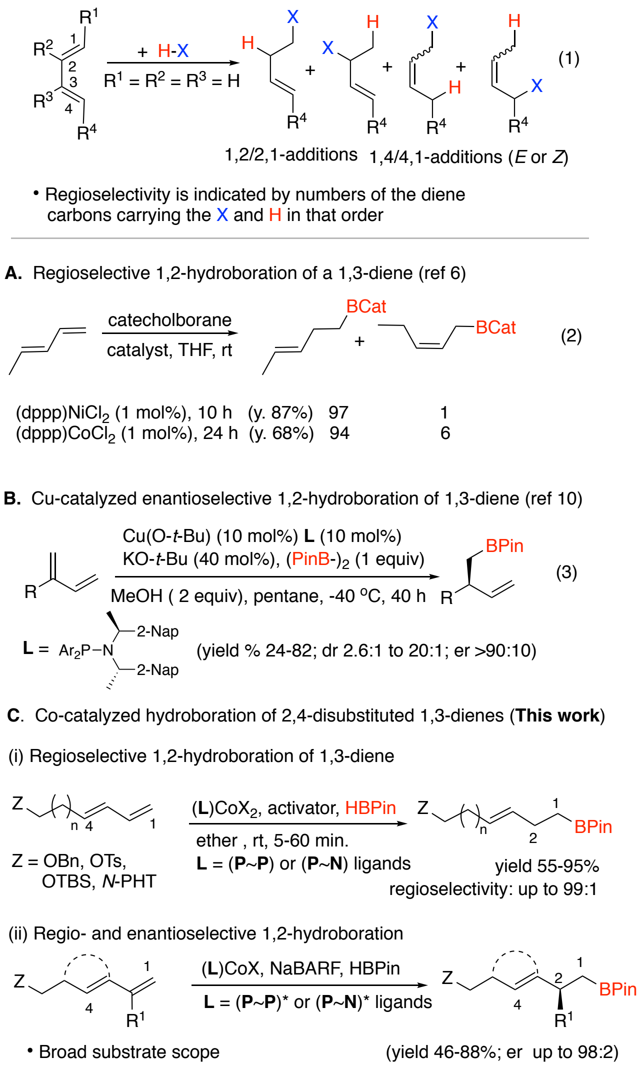


Figure 1. Selectivity in hydroboration of 1,3-dienes

Our interest in this problem had its origin in the cobalt catalysis of enantioselective diene-alkene heterodimerization reactions. During these investigations we identified what appeared to be Co(I)-species, generated by treatment of (**L~L**)CoX$_2$ [(**L~L**) = 1,n-*bis*-diphenylphosphinoalkane)] with either trimethylaluminum, or, with zinc and NaBARF [(BARF = *tetrakis*-[(3,5-*bis*-trifluromethyl)phenyl]borate)], as catalysts for highly efficient regio- and enantioselective codimerizations of prototypical 1,3-dienes and ethylene.[1h,12] The Zn/NaBARF-mediated reactions also work for heterodimerization of 1,3-dienes and acrylates.[1d] Isolated Co(I) complex (dppp)$_3$Co$_2$Br$_2$ in the absence of an activator *does not* catalyze these dimerization reactions. However, in the presence of activators like NaBARF or (C$_6$F$_5$)$_3$B a quantitative reaction ensues.[1d] We wondered if these catalyst systems would also effect selective hydroboration reactions of 1,3-dienes. The studies that followed revealed several novel aspects of this venerable reaction (Figure 1**C**), including a possible role of a cationic Co(I)-catalyst, the details of which are reported here.

RESULTS AND DISCUSSION

Selective 1,2-Hydroboration of 1,3-Dienes. Our early studies concentrated on the reaction between a prototypical 1,3-diene, (*E*)-1,3-nonadiene (**1a**) and pinacolborane (HBPin, Pin = 2,3-dimethylbutane-2,3-dioxy) in the presence of 5 mol% of (**L**)CoCl$_2$ [**L** = *bis*-1,n-diphenylphosphinoalkane, n = 1-5, Figure 2) and various activators/reducing agents at room temperature to give 2 major products **2a** (a 1,2-adduct) and **3a** (a 1,4-adduct), along with 0-5% of an isomerization product **4a** (Eq 4, Table 1).[13] In sharp contrast to catecholborane,[6] HBPin showed no reactivity with dienes in the presence of Co(II)-complexes *without* an activator such as trimethylaluminum (TMA) or methylaluminoxane (MAO) (Eq 4, Table 1, entries 1-3 vs entries 4 and 5). A quick optimization of activators and solvents (Table 1)[13] revealed that for the formation of the 1,2- and 1,4-adducts (**2a** and **3a**), methyl aluminoxane (MAO) in methylene chloride or ether was the most suitable solvent (entries 4 and 5), with the latter giving slightly better regioselectivity (**2a**:**3a** = 95:5) for the 1,2-addition.[13]

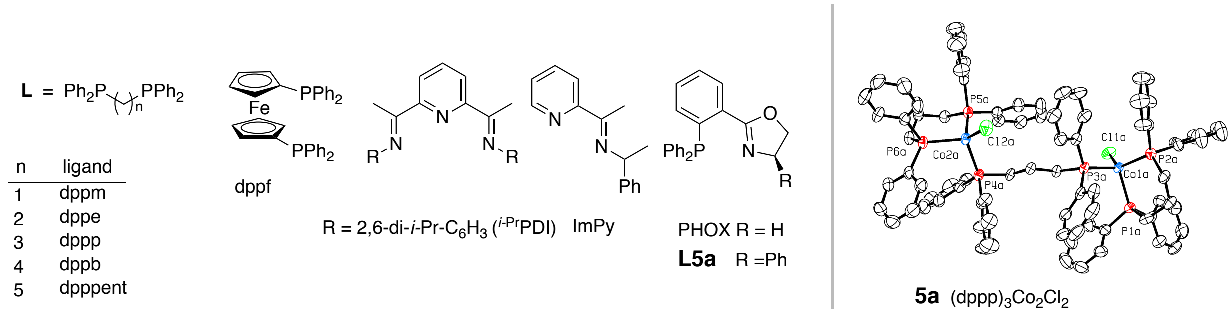
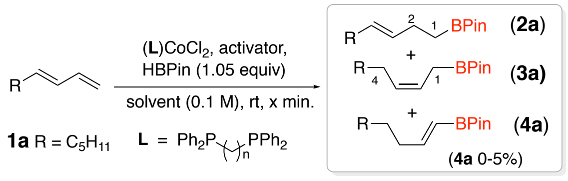


Figure 2. Ligands and Co(I) complex used in scouting experiments (Tables 1 and 2)



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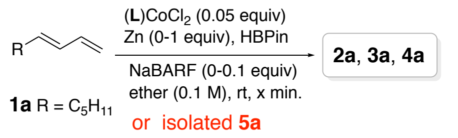


(5)

Compared to MAO, TMA gave lower selectivity (entry 4 vs entry 8). 1,2-Dimethoxyethane and THF were acceptable (entries 6 and 7, see also Table S1, p. S19 in Supporting Information). But the reaction rate was significantly lower (up to 18 h for complete reaction versus 5 min for ether or CH_2Cl_2 under otherwise similar conditions). Several other aluminum salts, Grignard reagents and NaB(H)Et_3, commonly used for activation of Co(II) complexes in catalytic hydrofunctionalization reactions, were ineffective (entry 18, see also Table S2, p. S20). When there was no hydroboration, minor products resulting from isomerization and/or reduction of the starting material were observed.

Table 1. Effect of Activators, Solvents on (dppp)Co(I)-Catalyzed Hydroboration of (*E*)-1,3-Nonadiene (1a)[a]

entry	catalyst (mol%)	activator (equiv.)	Zn (equiv.)	solvent	time	conv. (%)	**2a:3a:4a**
1	0	0	0	ether	44 h	0	-
2	10	0	0	ether	44 h	0	-
3	0	MAO (2)	0	CH_2Cl_2	2.5 h	0	-
4	5	MAO (2)	0	CH_2Cl_2	5 min	100	90:10:0
5	5	MAO (2)	0	ether	5 min	100	95:5:0
6	5	MAO (2)	0	DME	20 h	100	94:6:0
7	5	MAO (2)	0	THF	18 h	100	95:5:0
8	10	TMA(0.3) [b]	0	CH_2Cl_2	15 min	100	46:54:0
9	5	MAO (2)	0	$PhCH_3$	20 h	0	--
10	5	NaBARF (0.1)	1	ether	30 min	100	82:14:4
11	5	$AgSbF_6$ (0.1)	1	ether	2 h	100	68:32:0
12	5	NaBARF (0.1)	0	ether	30 min	88	82:13:5
13	5	$InBr_3$ (0.1)	1	ether	30 min	100	73:19:7
14	5	0	1	ether	24 h	<5	-
15	Co(I): **5a** [c]	NaBARF (0.04)	0	CH_2Cl_2	5 min	100	83:14:3
16	Co(I): **5a** [c]	NaBARF (0.04), -20 °C	0	CH_2Cl_2	45 min	100	89:11:0
17	Co(I): **5a** [c]	0	0	CH_2Cl_2	24 h	0	--
18	5	Various[d]	-	CH_2Cl_2	0.5-2 h	0	--

[a] See Eq 4 (entries 1~9) and 5 (entries 10~17) for typical procedures (see Supporting Information p, S16 for details). Catalyst (dppp)$CoCl_2$ used unless otherwise noted (entries 15 -17). See Supporting Information for further details. [b] Me_3Al at -10 °C. [c] Recrystallized Co(I) complex $Co_2(dppp)_3Cl_2$ (**5a**) used (1 mol%). [d] (dppp)$CoCl_2$ with $AlCl_3$, Et_3Al, $EtAlCl_2$, Et_2AlCl, Me_2AlCl, EtMgBr, or NaB(H)Et_3 (all at rt). See Table S2 (p. S19) for further details.

We also discovered that a more functional-group tolerant catalyst system that effected heterodimerization of 1,3-dienes and alkyl acrylates[1d] was competent to effect the regioselective hydroboration reactions of 1,3-dienes (Eq 5 and Table 1, entries 10-17), even though the 1,2:1,4-selectivity is slightly lower (~82:14) compared to the MAO-activated catalysts.[13] Thus a combination of (dppp)$CoCl_2$ (0.05 equiv), 1 equiv of activated Zn and 0.1 equiv of NaBARF gave a mixture of **2a**, **3a** and **4a** in a ratio 82:14:4 (entry 10; For further details, see also Tables S4-S7 in Supporting Information, p. S22). Under these conditions, proportion of the isomerization product **4a** increases progressively with time, suggesting that it is indeed a secondary (isomerization) product. Replacement of NaBARF with $AgSbF_6$ (0.1 equiv) led to a slow reaction (2 h) giving a ratio of 68:32 for **2a** to **3a** (entry 11). While Zn alone (*in the absence of NaBARF*) is not capable of effecting the reaction (entry 14), surprisingly, NaBARF (*in the absence of Zn*) appears to give the products in a relatively slow, yet clean reaction (entry 12), presumably HBPin acting as a reducing agent to produce a competent Co(I)-catalyst.[8a,b] $InBr_3$ can be used as a replacement for NaBARF, with some deterioration of regioselectivity (entry 13).

In order to verify the role of a cationic Co(I)-intermediate in these processes, we synthesized and fully characterized (X-ray crystallography) a Co(I)-complex $(dppp)_3Co_2Cl_2$ (**5a,** Fig 2) and used this *isolated* complex for hydroboration studies.[13] As expected, the isolated complex **5a** (0.01 equiv) in the presence of NaBARF (0.04 equiv) proceeded to give an exceptionally clean, fast reaction (entry 15). Even at -20 °C this complex (1 mol%) effected quantitative hydroboration of the diene in ~ 45 min (entry 16). *The Co(I) complex **5a** in the absence of NaBARF showed no activity for several hours (entry 17).* Among hydrocarbon solvents, toluene was unsuitable, leading to a complex reaction; hexane gave the three products in a ratio of 85:12:2.

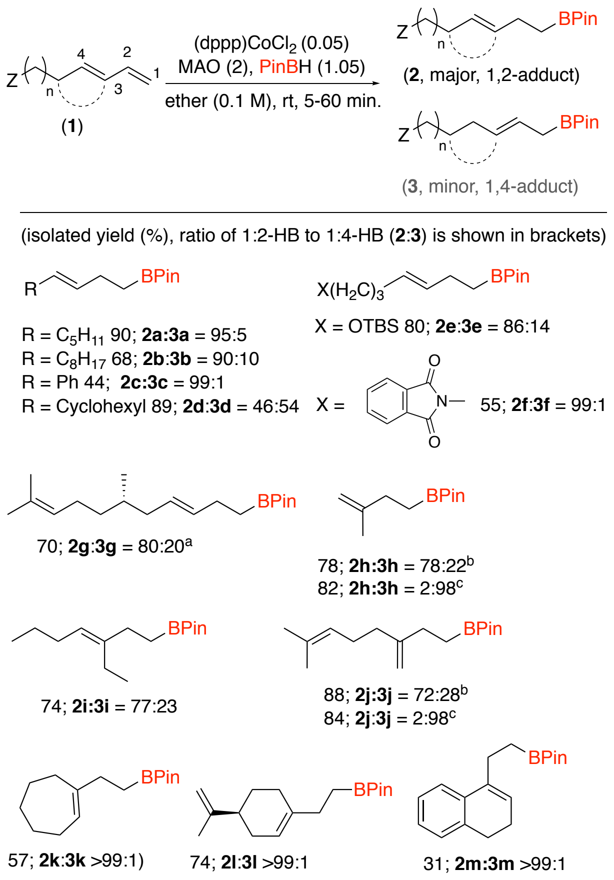
Ligand Effects. Further studies revealed that the regioselectivity of the reaction is strongly dependent on the nature of the ligand. In several instances significantly more of a vinylboronate **4a**, resulting from isomerization of the initial adducts, is also formed, especially with ligands dppm, dppe, dppb and dppf (Table 2, see also Table S3 for a more complete list, p. S21). The reaction with ligands with narrow bite angle (dppm and dppe) gave 1,4-adduct (**3a**) as the major product (Table 2, Entries 1 and 2). The iminopyridine ligands (see Fig 2 for the structures of the ligands)) were included in this study (entries 7 and 8) since they have been previously used in both Co- and Fe-catalyzed hydroboration reactions.[2b,5c,7,14]In the event, reduced cobalt complexes of these imine ligands promoted only relatively sluggish non-selective reactions (entries 7 and 8). Yet another imine-type ligand we tested, phosphino-oxazoline, PHOX and a phenyl-substituted analog **L5a**,[15] (see Fig 2 and Fig 4 for structures of ligands) also gave predominantly the 1,4-hydroboration product upon activation by Zn and NaBARF (entries 9 and 10).

Table 2. Effect of Ligands on Regioselectivity of Hydroboration of (*E*)-1,3-Nonadiene (1a)[a,b]

entry	catalyst (5 mol%)	activator, (equiv)	solvent	time	conv. (%)	**2a**:**3a**:**4a**[c]
1	(dppm)$CoCl_2$	MAO (2)	Et_2O	4 h	100	6:82:12
2	(dppe)$CoCl_2$	MAO (2)	Et_2O	3 h	100	15:70:15
3	(dppp)$CoCl_2$	MAO (2)	Et_2O	15 min	99	>95:5:0
4	(dppb)$CoCl_2$	MAO (2)	Et_2O	3 h	100	71:19:10
5	(dpppent)$CoCl_2$	MAO (2)	Et_2O	20 h	80[d]	100:0:0
6	(dppf)$CoCl_2$	MAO (2)	Et_2O	3 h	100	58:21:21
7[b]	($^{i\text{-Pr}}$PDI)$CoCl_2$	$NaBHEt_3$ (0.3)	Et_2O	24 h	56[d]	41:59:0
8[b]	(ImPy)$CoCl_2$	$NaBHEt_3$ (0.2)	THF	24 h	57[d]	32:68:10
9	[**PHOX**]$CoBr_2$	Zn (1), NaBARF (0.1)	Et_2O	25 min	100	30:70:0[e]
10	[**L5a**]$CoBr_2$ (R = Ph)	Zn (1), NABARF (0.1)	Et_2O	25 min	100	9:89:1

[a] See Eq. 4 (entries 1-8) and Eq 5 (entries 9, 10) and Supporting Information for details and a more complete set of Co(II)-complexes. [b] See Eq 4 and 5, and, Figures 2 and 4 for structures of ligands. [c] Determined by GC where base-line separations of the isomers were observed. [d] Remaining material was reduction or isomerization of starting diene. [e] In 24 h the ratio changed to 40:36:24.

The scope of the reaction for a series of dienes[4b] was explored under the optimized reaction conditions [Eq 4, Table 1, entry 5: (dppp)$CoCl_2$/MAO/ether/rt] and the results are shown in Fig 3. In most cases the reaction was complete with 5 mol% catalyst in ether (0.1 M) as the solvent within 60 min leading to the terminal boronate (**2**) resulting from 1,2-hydroboration. Higher proportions of the 1,4-adducts were obtained in substrates carrying a relatively bulky 4-subsituent (**2d**:**3d** = 46:54; **2g**:**3g** = 80:20). 3,4-Dialkyl 1,3-diene also gave higher amounts of 1,4-adduct (e.g., **2l**:**3l** = 77:23). The product distribution form isoprene and myrcene, two dienes with 2-substituents is particularly noteworthy for the ligand dependence on the ratio of the 1,2- vs 1,4-adducts. With (dppp)$CoCl_2$, isoprene gave a ratio of **2h**:**3h** = 78:22, whereas myrcene gave a ratio of **2j**:**3j** = 72:28. Both these substrates gave an uncommonly high selectivity for the 1,4-adduct (**2h**:**3h** = 2:98; **2j**:**3j** = 2:98) with the phosphinooxazoline ligand **L5d**. The reaction works well with 1-vinylcycloalkenes giving high proportion of the 1,2-hydroboration products (e.g., **2k**, **2l**, **2m**). The reaction was tolerant of common functional groups, among them, the following groups: TBS-ether (**2e**), *N*-phthalimido group (**2f**), and di- and trisubstituted alkene (**2g**, **2j, 2l**). We also noticed that the regioselectivity of the reaction was dependent on the geometric isomeric purity of the starting diene. For example, isomerically pure (3*E*)-(6*R*)-6,10-dimethyl)undeca-1,3-9-triene gave the product **2g**:**3g** with >80:20 selectivity for the 1,2:1,4-additions; however for a mixture of geometric isomers of (3*E*)- [(6*R*)]- and (3*Z*)-(6*R*)-triene (44:56), a lower selectivity for the adducts was observed.



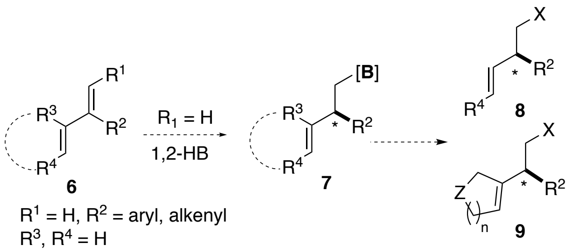
a. From (3*E*)-6-(*R*)-6,10-dimethyl)undeca-1,3-9-triene
b. From Procedure F using ligand dppp (See SI, p. S29-S30)
c. From Procedure F using ligand **L5d** (See SI, p. S29-S30)

Figure 3. Scope of regioselective 1,2-hydroboration of 1,3-dienes. See Figure S1 (Supporting Information, p. S6) for structures of precursor 1,3-dienes.

1,2-Hydroboration of 2-substituted dienes. Next our attention turned to how we might exploit the novel regioselectivity afforded by the cobalt catalysts for an enantioselective reaction. We reasoned that among the various prochiral dienes, novel and most impactful for this purpose would be 2,4-disubstituted 1,3-dienes (**6**), which can optionally include a 3-substituent (Scheme 1). Such a substitution pattern would also include R^3 and R^4 substituents as parts of a carbocyclic or heterocyclic ring system. The products that could be derived from resulting boronate (**7**) will include an impressive array of chiral intermediates generically represented by **8** and **9** (X = -OR, -NHR, -alkyl, -alkenyl, -aryl, -halogen).

Our studies started with a preliminary evaluation of cobalt-catalyzed hydroboration of three prototypical 2-substituted 1,3-dienes, **10a-c** (Scheme 2) using the protocols outlined in Eq 4 (**L**CoX$_2$, MAO activation) and Eq 5 (**L**CoX$_2$, Zn/NaBARF activation). Of these, we chose the 2-ethyl diene **10b** for a detailed optimization for high selectivities for the formation of the major chiral 1,2-adduct (**11b**) since this substrate proved the most challenging. Like the other 2-substituted dienes, **10b** gave one major boronate regioisomer (up to 97% of the mixture of boronates), **11b**, along with two minor products, **12b** and **13b**, corresponding to 1,2-, 1,4- and 4,3-addition of HBPin to the diene (Scheme 2). A selection of the most pertinent results from these studies are shown in Table 3.[16] The Supporting Information contains a more elaborate table, Table S8 (p. S24) with extensive details of optimization of ligands, activators and reaction parameters for high selectivity for the formation of the 1,2-hydroboration product, **11b**. These experiments revealed that among the achiral 1,n-*bis*-diphenylphosphino-ligands (Figure 4 for structures of various ligands[17]) only 1,3-*bis*-diphenylphosphinopropane (dppp) gave preparatively useful levels of regioselectivity (**11b**: 92-95%) between the three isomers (**11b, 12b** and **13b**).[18,19] Isolation of the boronates resulted in some losses on the column and the isolated yields are sometimes lower than the assays by GC or NMR. Consequently, the crude products were converted into the corresponding alcohols by oxidation with H$_2$O$_2$ for further analysis and identification.

Scheme 1. 1,2-Hydroboration of Substituted 1,3-Dienes



Scheme 2. Selective 1,2-Hydroboration of 2-Substituted 1,3-Dienes

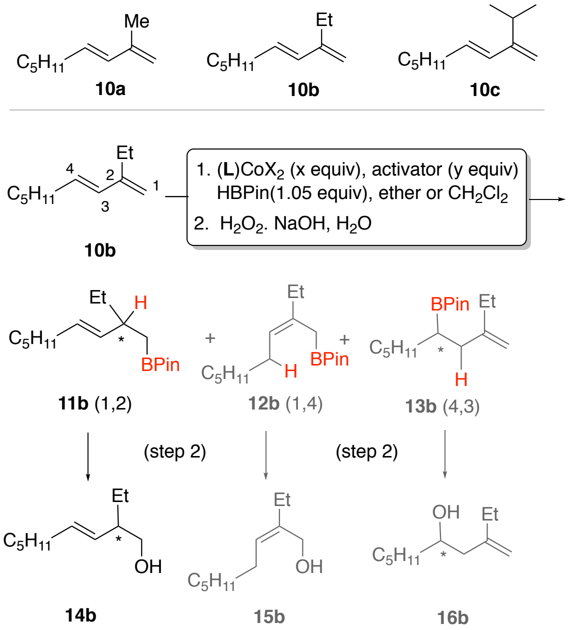


Table 3. Optimization of Regio- and Enantioselectivity in Hydroboration of 10b[a]

entry	[**L**]Co-complex (mol%)	activator (mol%)	Zn (mol%)	time (min)	conv. (%)[b]	**11b**:**12b**:**13b**[b]	er[c] **14b** (*S*)
1	(dppp)CoCl$_2$ (5)	NaBARF (10)	100	25	100	92:1:4	50:50
2	**5a**: (dppp)$_3$Co$_2$Cl$_2$ (1) (recrystallized)	NaBARF (4)	0	5	100	95:2:3	50:50
3	(PHOX)CoBr$_2$ (5)	NaBARF (10)	100	25	100	97:3:0	50:50
4	(*S*,*S*)-(BDPP)CoBr$_2$ (5)	NaBARF (10)	100	2 x 60	100	63:0:37	92:8[d]
5	**5b**: [(*S*,*S*)-(BDPP)]$_3$Co$_2$Cl$_2$ (1) (recrystallized)	NaBARF (4)	0	20	100	65:0:35	93:7[d]
6	(**L4a**)CoCl$_2$ (5)	NaBARF (10)	100	60	100	97:1:2	90:10[e]
7	(**L4b**)CoBr$_2$ (5)	NaBARF (10)	100	60	75	57:43:0	70:30
8	(**L4c**)CoBr$_2$ (5)	NaBARF (10)	100	24 x 60	15	90:10:0	80:20
9	(**L5a**)CoCl$_2$ (5)	MAO (200)	0	7.5 x 60	100	93:4:3	78:22
10	(**L5a**)CoCl$_2$ (5)	NaBARF (10)	100	25	100	96:0:4	93:7
11	(**L5a**)CoCl$_2$ (5)	NaBARF (10)	0	6 x 60	100	93:3:4	92:8
12	(**L5a**)CoCl$_2$ (5)	0	0	24 x 60	0	--	--
13	(**L5c**)CoBr$_2$ (5)	NaBARF (10)	100	30	100	94:0:5	94:6
14	(**L5d**)CoBr$_2$ (5)	NaBARF (10)	100	6 x 60	100	97:0:2	94:6
15	(**L6c**)CoBr$_2$ (5)	NaBARF (10)	100	20	100	91:2:7	62:38
16	(**L7**)CoBr$_2$ (5)	NaBARF (10)	100	45	100	95:5:0	53:47

[a] See Scheme 2 and Supporting Information for experimental details and analytical data. A more elaborate table (Table S8, p. S24) with additional ligands and procedures can also be found in the SI. [b] Determined by GC and confirmed by ^{1}H NMR. [c] For **11b**. Determined by CSP GC of the alcohols (**14b**) prepared by oxidation (basic H$_2$O$_2$) of the boronates **11b**. Configuration confirmed by comparison of optical rotation of **14b** that of an authentic sample. See Supporting Information for details. [d] Selectivities for the minor product (**13b**): entry 4 (er = 98:2, *S* major); entry 5 (er = 98:2, *S* major). See Supporting Information for details. [e] In this case, the absolute configuration of the major product is (*R*).

The best results were obtained from activation of the (dppp)CoCl$_2$ by reduction with zinc (1 equiv) in the presence of NaBARF (10 mol%, Table 3, entry 1). Use of isolated (recrystallized) Co(I)-complex (dppp)$_3$Co$_2$Cl$_2$ (**5a**, Figure 2) in the presence of NaBARF resulted in the fastest and cleanest reaction (5 min, 1 mol% Co(I) catalyst vs 25 min, 5 mol% in situ generated Co(I) catalyst, entry 1 vs entry 2) under otherwise identical conditions to give comparable selectivity for the major isomer **11b** (see also entry 15, Table 1 for similar reaction with (*E*)-nona-1,3-diene). The Co(II)-complex derived from achiral PHOX ligand (Figure 4) was also found (entry 3) to be slightly more selective for the production of the 1,2-adduct (**11b**:**12b**:**13b** = 97:3:0). This surprising finding is in sharp contrast to the corresponding reaction between HBPin and 1,3-dienes with no substituents at C$_2$ such as (*E*)-1,3-nonadiene (**1a**) where the cobalt complex of this ligand led to a non-selective reaction with formation of a 1,4-adduct as the major product (Table 2, entry 9).

Enantioselective 1,2-hydroboration of 2-substituted dienes. Enantioselective hydroboration of **10b** was further explored under the newly developed protocols (Scheme 2) using various chiral ligands and the results are shown in entries 4-16 in Table 3. Structures of some of the chiral ligands and that of a fully characterized (X-ray crystallography) Co(I)-complex, [[(*S*,*S*)-BDPP]$_3$Co$_2$Cl$_2$], used in this study are shown in Figure 4.[17] The products **11b**, **12b** and **13b** resulting from the 1,2-, 1,4-, and 4,3-hydroborations (Scheme 2) were oxidized to the corresponding alcohols (**14b**, **15b** and **16b**). Enantioselectivity for the major chiral alcohol products **14b** and **16b** (the latter mostly seen only in entries 4 and 5) were determined by chiral stationary phase gas chromatography (CSP GC). In cases where these alcohols showed poor resolution on CSP GC, chiral stationary phase liquid chromatography (CSP HPLC) of the corresponding 2-naphthoate esters were used for the er determination.[19] The absolute configurations among these series of alcohols were established by comparison of specific rotations with those of authentic samples (see Supporting Information).

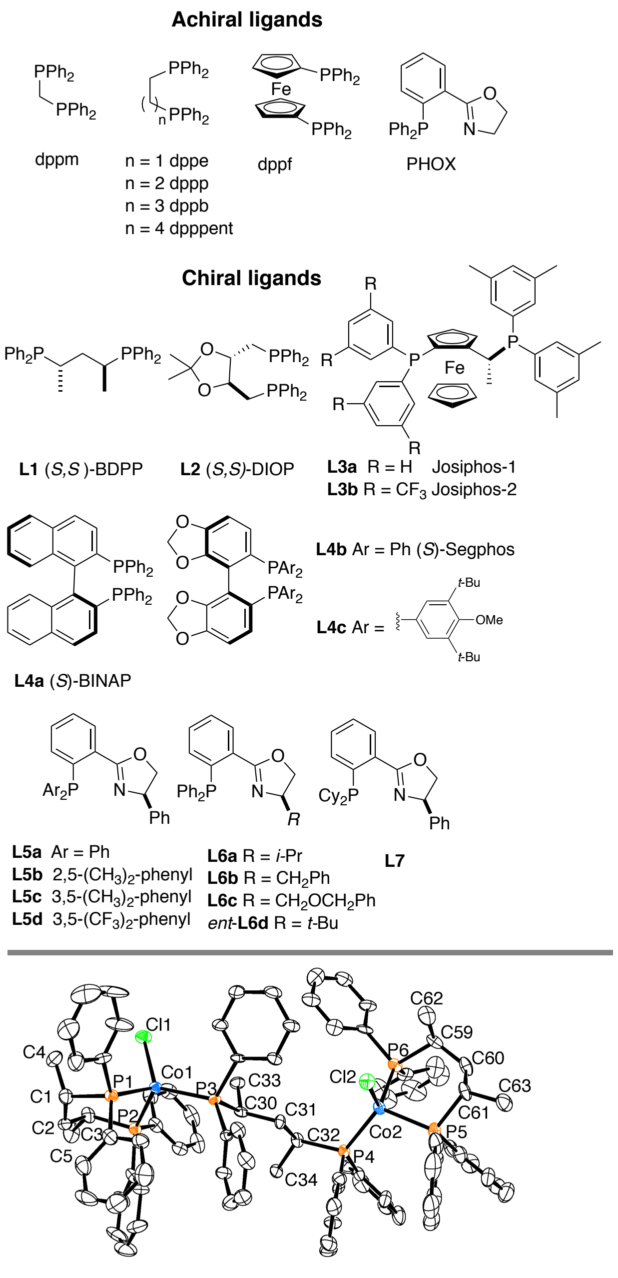
Among the initially studied cobalt complexes, [(*S*,*S*)-BDPP]CoBr$_2$,[1m] (5 mol%) in the presence of Zn (1 equiv) and NaBARF (10 mol%) was found to be an efficient catalyst for the enantioselective reaction, giving exclusively the chiral products, the 1,2-adduct **11b** (63%) and the 4,3-adduct **13b** (37%) in very good to excellent enantioselectivities (er = 92:8 and 98:2 respectively for the two adducts, entry 4).[20] The corresponding pre-reduced Co(I)-complex **5b** {[(*S*,*S*)-BDPP]$_3$Co$_2$Cl$_2$}, 1 mol%, Figure 4] in the presence of 4 mol% NaBARF was also an exceptional catalyst exhibiting similar regio- and enantioselectivities (entry 5). As expected from earlier results on the hydroboration of (*E*)-1,3-nonadiene using the isolated Co(I) complex (dppp)$_3$Co$_2$Cl$_2$ (Table 1, entry 17), there was *no reaction in the absence of NaBARF*. Selectivities of 2,2'-biaryl-*bis*-diphenylphosphine-Co(II) complexes (**L4a**, **L4b** and **L4c**) depend on the structures of the ligands, with the BINAP-ligand giving overall the best regio- and enantioselectivities [97% 1,2-HB with er = 90:10 (entry 6)].[17] The segphos-complex gave significantly larger proportion of the 1,4-adduct and only a modest enantioselectivity for the 1,2-adduct **11b** (entry 7, **11b**:**12b** = 57:43; er for **11b**: 70:30).

Achiral and chiral phosphino-oxazoline ligands[15] are by far the best ligands for obtaining the highest regio- and enantioselectivities in the formation of the 1,2-hydroboration product **11b** (entries 3 and 9-14). Among the chiral ligands, the (*R*)-4-(phenyloxazolinyl)-diphenylphosphino-ligand **L5a** (entry 10) and a corresponding *bis*-(3,5-dimethylphenyl) ligand **L5c** (entry 13) are by far the best, the latter giving er values 94:6 for the 1,2-adduct, **11b**. A structurally analogous *bis*-(3,5-*bis*-trifluoromethylphenyl) ligand **L5d** is equally good, even though the reaction is slower (entry 14). Activation by Zn and NaBARF appears to be superior to MAO (entry 9 vs 10). Other ligands in this class (**L5b**, **L6a-d**, **L7**) all gave poor results.[16]

From a practical perspective, the enantioselective 1,2-hydroboration of a 2-substituted diene using HBPin is best carried out using the reduced (**L5a**)CoX (X = Cl, Br), a catalyst generated by in situ reduction of the corresponding (**L5a**)CoX_2 complex with Zn in the presence of NaBARF (Scheme 3, see SI p. S17, procedure D for details). This protocol is broadly applicable as illustrated by examples shown in Figure 5. Even though the isolated Co(I)-complex activated with near equivalent amount of NaBARF is significantly more active (typically the reaction is complete within 5 min with 1 mol% catalyst), the in situ reduction procedure avoids the isolation of the sensitive Co(I)-complex. The reactions are easily scaled up to gram scales with no loss of selectivity.

In addition to the products from simple 1,3-dienes[4b] with primary or secondary alkyl substituents at C_2 and/or C_4 positions of the diene (products **11a -11f**), various other derivatives, a TBS ether (**11g**), a benzyl ether (**11h**), a tosylate (**11i**) and even a phthalimido group tolerated these mild reaction conditions to give excellent regio- and enantioselectivities (er generally > 94:6) for the 1,2-hydroboration products. 1-Alkenylcycloalkenes, which gave products (**11k-11n**) with an exocyclic chiral center, and, a latent endocyclic double bond for further elaboration.[21] A trisubstituted alkene derived from (*S*)-perrilaldehyde gave a product (**11o**) with excellent diastereoselectivity (96:4).

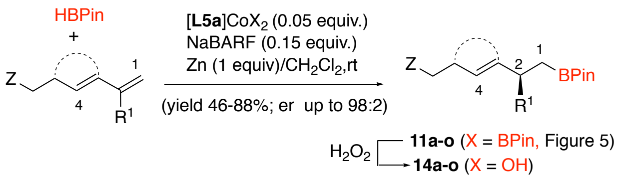
Cyclohexa-1,3-diene, the only endocyclic 1,3-diene in our study, with the *bis*-(3,5-di-trifluromethylphenyl)-PHOX ligand **L5d**, gave a 1,4-adduct (*R*)-**12p** [22] with er >95:5 (1,2:1,4-adduct 3:97). [(*R*)-BINAP]$CoBr_2$ gave mostly the 1,2-adduct (**11p**)[11] in a surprisingly low er of 69:31. An examination of the dependence of the enantioselectivity on the enantiomeric purity of the BINAP ligand show that there is no nonlinear effect on the selectivity in this reaction unlike what was seen in a related Cu-catalyzed reaction (See Supporting Information for details).[10a] As for the limitations, a diene with a bulky 4-substituent, **10q**, gave a product with noticeably low er of 74:26 for the 1,2-adduct **11q** in only 48% yield.

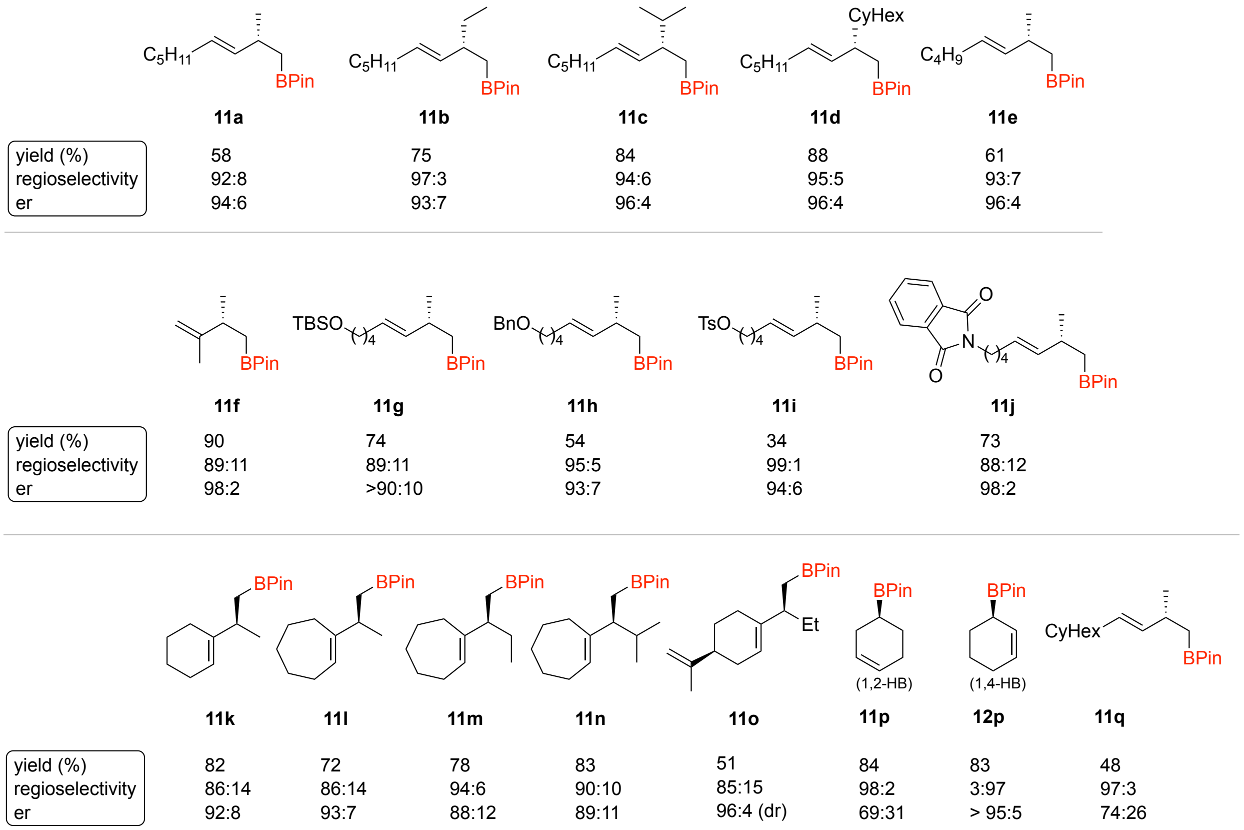


5b [(*S*,*S*)-BDPP]$_3$Co$_2$Cl$_2$

Figure 4. Achiral and chiral ligands and a chiral Co(I) complex for regio- and enantioselective hydroboration of prochiral 1,3-diene

Scheme 3. Regio- and Enantioselective Hydroboration of Prochiral 1,3-Dienes





	11a	**11b**	**11c**	**11d**	**11e**
yield (%)	58	75	84	88	61
regioselectivity	92:8	97:3	94:6	95:5	93:7
er	94:6	93:7	96:4	96:4	96:4

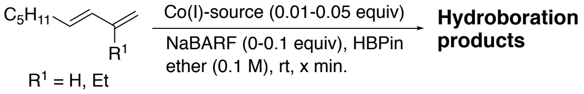
	11f	**11g**	**11h**	**11i**	**11j**
yield (%)	90	74	54	34	73
regioselectivity	89:11	89:11	95:5	99:1	88:12
er	98:2	>90:10	93:7	94:6	98:2

	11k	**11l**	**11m**	**11n**	**11o**	**11p**	**12p**	**11q**
yield (%)	82	72	78	83	51	84	83	48
regioselectivity	86:14	86:14	94:6	90:10	85:15	98:2	3:97	97:3
er	92:8	93:7	88:12	89:11	96:4 (dr)	69:31	> 95:5	74:26

Figure 5. Scope of enantioselective 1,2-hydroboration of substituted 1,3-dienes. See Supporting Information for details including the structures of the starting 1,3-dienes (Figure S2, p. S6). For typical procedure, see procedure D (p. S17, Supporting Information). Column under each compound shows isolated yields, regioselectivity and enantioselectivity (er) in that order. Boronates (*S*)-**11p** [11] (a 1,2-adduct, formed with *ent*-**L4a** as the ligand) and (*R*)-**12p** [22] (formed with **L5d** as the ligand), have been reported before. See Supporting Information for details.

Role of Cationic Co(I) in Hydroboration of 1,3-Dienes and a Possible Mechanism of the Reaction. Even though we have not carried out any detailed mechanistic studies, several observations made during the optimization studies provide key insights into the mechanism of this reaction, for which many details are already available in the literature for both the Cu and Co-catalyzed versions.[3c,7-8,23]

The key results that are pertinent to this discussion are assembled in Table 4 and further discussed below (Eq 6). In a series of experiments with reducing agents and activators, we find strong evidence that a cationic Co(I) may be involved as an intermediate in the reaction, just as they played a key role in the diene-acrylate dimerization, where we initially discovered this.[1d] Even though (dppp)CoCl$_2$ is known to be a catalyst, albeit a poor one, for the hydroborations using catechol borane,[6] this complex does not effect the reactions of HBPin in the absence of an activator/reducing agent such as MAO or Zn and NaBARF (entries 1 vs 2 and 3). The Zn/NaBARF-activation works best when 1 equivalent of Zn and 0.1 equivalent of NaBARF are employed (entry 3). Surprisingly, while Zn alone is *not competent* to effect (apparently the ZnBr$_2$ that is produced is an inefficient Lewis acid to promote the reaction) the hydroboration (entry 5), NaBARF alone *does activate* the Co(II)-salts in a slow reaction (entry 4). In this reaction, NaBARF presumably plays a dual role, one, to promote the reduction of the Co(II) salt by HBPin, and, two, to generate a Co(I)-cationic species from the reduced cobalt salt thus generated. Support for such a hypothesis comes from the fact that independently synthesized, and a fully characterized (X-ray crystallography) Co(I)-complexes (dppp)$_3$Co$_2$Cl$_2$ (**5a**, Figure 2), or [(*S,S*)-BDPP]$_3$Co$_2$Cl$_2$ (**5b**, Figure 4) are NOT catalysts in themselves for the hydroboration (entries 7 and 9). However, upon addition of NaBARF the reaction is almost instantaneous (entry 6 and 8), a situation reminiscent of the Lewis acid activation of Rh(I)-catalyzed hydroboration of alkenes observed by Crudden.[23b] Indeed the use of isolated Co(I)- complexes in conjunction with NaBARF represent the most efficient way of conducting this hydroboration reaction, which we found especially valuable for carrying out the enantio-



(6)

Table 4. Role of Cationic Co(I)-Catalyst in Hydroboration of Dienes[a]

entry	Co(I)-source (equiv)	Zn (equiv)	NaBARF (equiv)	MAO (equiv)	time (min)	conver. (%)
1	(dppp)$CoCl_2$ (0.05)	0	0	0	44 x 60	0
2	(dppp)$CoCl_2$ (0.05)	0	0	2	5	100
3	(dppp)$CoCl_2$ (0.05)	1	0.1	0	30	100
4	(dppp)$CoCl_2$ (0.05)	0	0.1	0	30	88
5	(dppp)$CoCl_2$ (0.05)	1	0	0	24 x 60	0
6	Co(I): $Co_2(dppp)_3Cl_2$ [b] (0.01)	0	0.1	0	5	100
7	Co(I)[b]: $Co_2(dppp)_3Cl_2$ (0.01)	0	0	0	24 x 60	0
8[c]	Co(I)[b]: Co_2[(*S*,*S*)-BDPP]$_3Cl_2$ (0.01)	0	0.04	0	20	100
9	Co(I)[b]: Co_2[(*S*,*S*)-BDPP]$_3Cl_2$ (0.01)	0	0	0	24 x 60	0

[a] See Eq 6 and Supporting Information (R = H, Et). [b] Recrystallized Co(I) complex **5a** or **5b** (See Figures 2 and 4 for structures). [c] Substrate (*E*)-2-ethyl-1,3-nonadiene, R = Et. (**L5a**)$CoCl_2$/Zn-mediated reactions also DO NOT proceed without NaBARF. See Supporting Information (pp. S284-286) for details.

selective reactions (Table 3, Figure 5). Temperatures as low as – 20 °C can be used to effect the 1,2-hydroboration of a 1,3-diene (Supporting Information, Table S7, p. S23). The configurations of the 1,2- and 1,4- hydroboration products, (*E* and *Z*) respectively, along with the remarkable solvent effects (e.g., significantly slower reaction in coordinating solvents such as THF and DME) also give some clues about the cationic nature of the putative intermediates in the reaction. In addition, several alternate well-defined Co(I) species prepared during our studies on diene-acrylate dimerization,[1d] e. g., [(*S*,*S*)-BDPP]Co(η^3-cyclooctenyl), (*S*)-BINAP]Co(η^3-cyclooctenyl), (dppp)Co(η^3-cyclooctenyl), when activated by $[H^+(OEt_2)_2[BARF]^-$, are also superb catalysts for this hydroboration, yielding similar selectivities. Based on our observations and literature precedents, we propose the mechanism outlined in Figure 6 for this reaction.

In this proposal, the reaction starts with the generation of the Co(I) species **17** by reduction of the (**P~P**)CoX_2 or (**P~N**)CoX_2 by Zn. This process may be assisted by NaBARF that is added to the reaction mixture. The fact that a sluggish reaction occurs even in the absence of Zn (*but only in the presence of NaBARF*) suggests that HBPin maybe competent to do this reduction under conditions where cationic intermediates can be generated. Abstraction of the halide from **17** by NaBARF generates a cationic species **18**, possibly stabilized by the 1,3-diene. Subsequent events are as yet uncertain, but it is reasonable to speculate that addition of HBPin followed by insertion of the terminal alkene into the Co-H bond in **19** in a 1,2-fashion (**L**Co[**B**] on C_1, H on C_2) would produce the intermediate **20a**. Reductive elimination[8a,23b,d] from this species would produce the 1,2-hydroboration product (**2**). Alternately, if the alkene inserts into the Co-B bond in a 2,1-mode[23c] (**L**Co[**H**] on C_2, B on C_1) a stabilized η^3-intermediate **20b** would result. Reductive elimination from **20b** with C-H bond formation can result in the 1,2- or 1,4-hydroboration product (**2** and **4** respectively). The configuration of the resulting double bond, (*E*) in the 1,2-adduct and (*Z*) in the 1,4-adduct is consistent with this conjecture. For the catalytic cycle in hydroboration, either an oxidative addition to Co(I)[8,23b,d] or a σ-bond metathesis[7,23a,c] has been invoked as a key step that activates the B-H bond of HBPin. In this discussion we have not considered alternatives involving the σ-bond-metathesis. Mechanistic studies to delineate these possibilities, and, the intriguing ligand effects [for example, why the major product from (*E*)-1,3-nonadiene (**1a**) using dppp ligand is the 1,2-adduct, whereas the Ph-PHOX (**L5a**) complex gives the 1,4-adduct exclusively) are currently in progress and will be reported in due course.

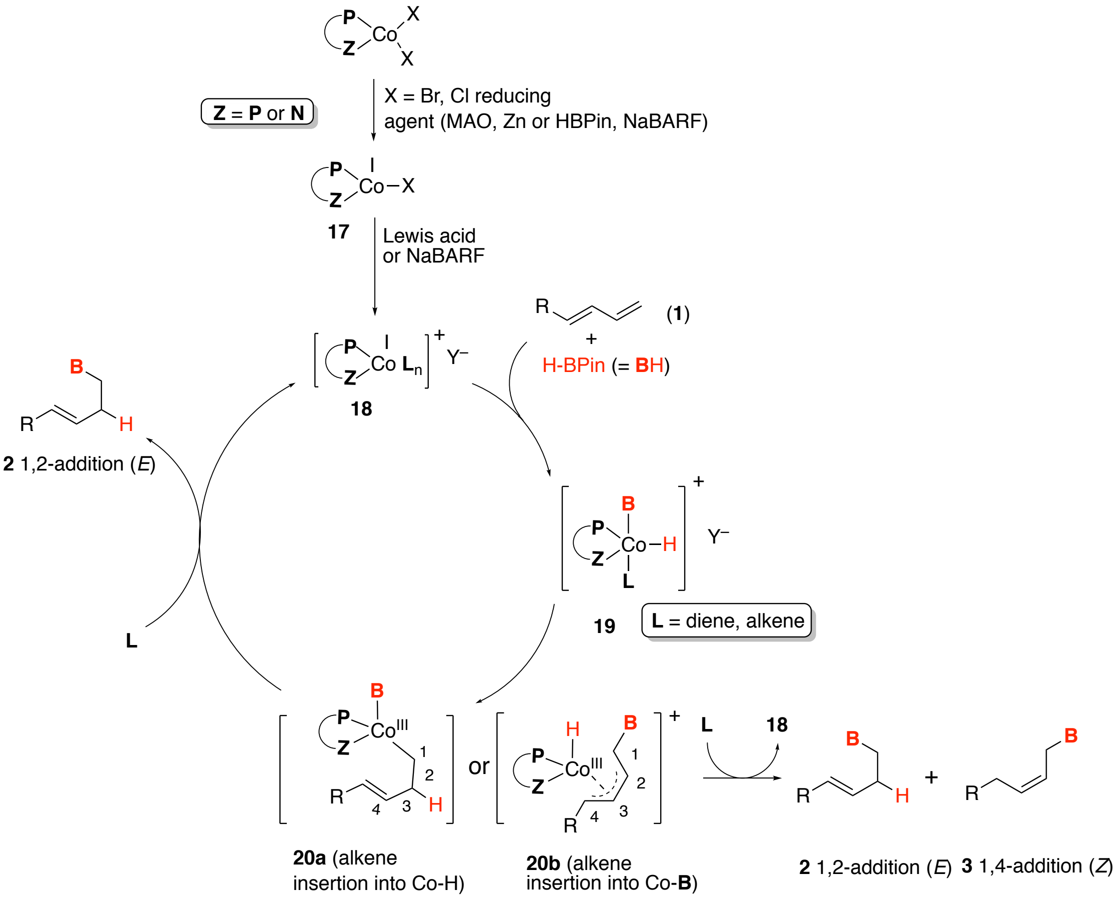
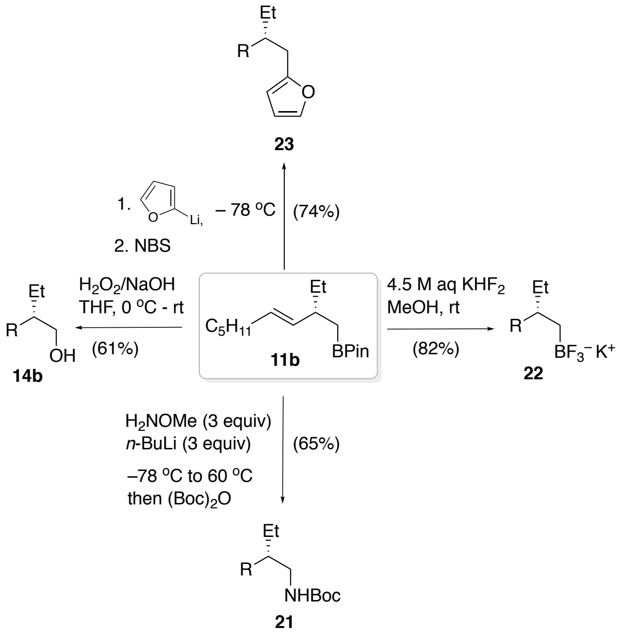


Figure 6. A plausible mechanism of the hydroboration of 1,3-dienes, which accounts for ligand, counter ion and solvent effects and configuration of products.

Useful transformations of the homoallylic boronates. Boronates are versatile compounds that are readily converted into other organic intermediates. In addition to the well-known basic H_2O_2-mediated oxidation to the corresponding alcohol, three other transformations of a prototypical boronate are shown in Scheme 4. The homoallylboronates have been converted into the corresponding alcohols, potassium trifluoroborate salts,[24] *N*-BOC amines[25] and aryl derivatives by *C*-BPin[26] to *C*-aryl transposition by known chemistry. Other examples of such compounds including alcohols derived from achiral (**2a** – **2m**) and chiral (**11a** – **11q**) boronates are included in the Supporting Information.

Scheme 4. Derivatization of Chiral Pinacolboronates



CONCLUSIONS

Among the myriad of possibilities for hydrofunctionalization reactions of 1,3-dienes, 1,2-hydroboration is an uncommon reaction. We find that reduced cobalt catalysts generated from 1,n-*bis*-diphenylphosphinoalkane complexes $[Ph_2P\text{-}(CH_2)_n\text{-}PPh_2]CoX_2$; n = 1~5) or from (2-oxazolinyl)phenyldiphenylphosphine complexes $[(PHOX)CoX_2]$ effect highly selective 1,2- and 1,4-additions of pinacolborane (HBPin) to a variety of 1,3-dienes. We have identified ligands that selectively execute these transformations with high regio- and enantioselectivities in 2-substituted dienes. The reactive catalysts can be generated from the cobalt (II)-salts using trimethylaluminum, methyl aluminoxane or activated zinc in the presence of NaBARF. The regioselectivity (1,2 vs 1,4) depends on the ligands and the diene, with $(dppp)CoX_2$ giving the best results (1,2:1,4 = >95:5) for both linear terminal 1,3-dienes and 2-substituted 1,3-dienes. Isolated and fully characterized (X-ray crystallography) Co(I)-complexes, $(dppp)_3Co_2Cl_2$ and $[(S,S)\text{-}BDPP]_3Co_2Cl_2$ *do not* catalyze the reaction unless activated by a Lewis acid or NaBARF, suggesting a key role for a cationic Co(I) species in the catalytic cycle. Regio- and enantioselective 1,2-hydroborations of 2-substituted 1,3-dienes are best accomplished using a catalyst prepared via activation of a chiral phosphine-oxazoline-cobalt(II) complex with zinc and NaBARF. A number of common functional groups, among them, -OBn, -OTBS, -OTs, *N*-phthalimido- groups, are tolerated and er's up to >98:2 are observed for several dienes including 1-alkenylcycloalk-1-enes.

ASSOCIATED CONTENT

Supporting information

This material is available free of charge via the Internet at http://pubs.acs.org

Experimental procedures, syntheses and isolation of all intermediates, and Tables with details of several optimization studies. Spectroscopic and gas chromatographic data showing compositions of products under various reaction conditions (PDF).
Crystallographic Information Files (.cif) for complex **5a**
Crystallographic Information Files (.cif) for complex **5b**.

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Notes

The authors declare no competing financial interest.

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(16) See Supporting Information (Table S8, p. S24) for more details.

(17) A complete list of all ligands examined is shown in Supporting Information (Figure S3, p. S15).

(18) The structure of the boronates were established by not only HRMS and rigorous NMR analysis of the primary products, but also those of the corresponding alcohols. The two enantiomeric alcohols are readily separted on CSP-GC, enabling the determination of enantioselectivity of the reaction.

(19) See Supporting Information for details of experiments, and spectroscopic and analytical details of the products, including achiral and chiral stationary phase chromatogarms.

(20) Incidentally, with the (*S,S*)-BDPP and (*S,S*)-DIOP ligands, unsubstituted 1,3-diene (*E)*-1,3-nonodiene (**1a**) also gave significant amount (~ 16%) of a 4,3-hydroboration product, structurally analogous **13**, in er's >91:9.

(21) For a discussion of the importance of configuration of exocyclic sterocenter next to a ring to which is attached the carbon carrying this center, and, some recent solutions to this problem, see: Tenneti, S.; Biswas, S.; Cox, G. A.; Mans, D. J.; Lim, H. J.; RajanBabu, T. V. "Broadly Applicable Stereoselective Syntheses of Serrulatane, Amphilectane Diterpenes, and Their Diastereoisomeric Congeners Using Asymmetric Hydrovinylation for Absolute Stereochemical Control", *J. Am. Chem. Soc.* **2018**, *140*, 9868-9881.

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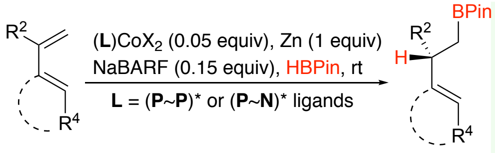
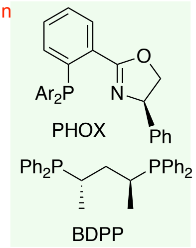
SYNOPSIS TOC





(er up to 98:2)

- Cyclic and acyclic 1,3-dienes
- Ligand-dependent regio- and enantioselectivity
- Functional group tolerant
- Cationic Co(I) intermediates