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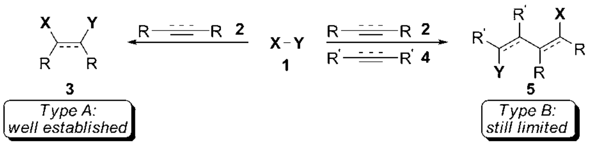
α-Chiral Allylsilanes

Nickel-Catalyzed Enantio- and Diastereoselective Three-Component Coupling of 1,3-Dienes, Aldehydes, and a Silylborane Leading to α-Chiral Allylsilanes[**]

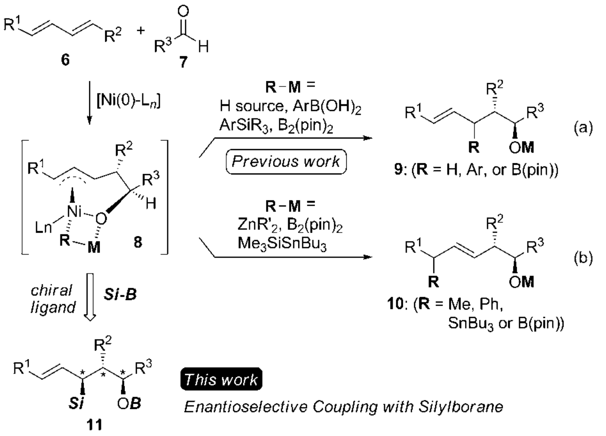
Nozomi Saito, Ayami Kobayashi, and Yoshihiro Sato**

Transition metal-catalyzed addition of the metal–metal linkage of bimetallic compounds (**1**: X, Y = B, Si, Sn, Ge, etc.) to unsaturated bonds (i.e., bismetalation) is an indispensable strategy for the synthesis of various types of organometallic compounds.[1] Bismetalation of simple unsaturated compounds **2**, such as alkenes, alkynes, and allenes, has been established as a promising method for the preparation of 1,2-dimetallo-organic compounds **3** (Scheme 1, type A). On the other hand, the multicomponent coupling of different unsaturated compounds **2** and **4** with a bimetallic reagent, wherein a C–C bond forming reaction accompanied by bismetalation occurs, should also be an attractive method to synthesize dimetallo compounds **5** (type B). Such an approach would give a wide variety of 1,*n*-dimetallo species by combining various types of bimetallic reagents **1** with unsaturated compounds **2** and **4**. However, in contrast to extensive studies that have been carried out on type A reactions, type B reaction systems are still limited and this coupling therefore remains a frontier in organometallic chemistry.[2] An enantioselective version of the type A bismetalation has also been extensively investigated as a practical method for the preparation of optically active organometallic compounds,[3] whereas an enantioselective type B multicomponent coupling has not been reported to date.[4]



Scheme 1. Transition-metal-catalyzed simple bismetalation of unsaturated compounds (Type A) and multicomponent coupling of unsaturated compounds with a bimetallic reagent (Type B).

Nickel-catalyzed intra- and intermolecular couplings of 1,3-dienes and aldehydes have attracted much attention because the coupling reaction has been recently employed as an efficient synthetic method for the generation of homo- and bis-homoallylic alcohols.[5,6] We have also contributed to the development of the field of nickel-catalyzed couplings and cyclizations of 1,3-dienes and carbonyl groups.[7,8] A key intermediate in diene–aldehyde coupling is oxanickelacycle **8**,[9] generated by the oxidative cycloaddition of 1,3-diene **6** and aldehyde **7** to a nickel(0) complex, which is known to react with various organometallic reagents.[10] Thus, transmetalation or σ-bond metathesis between nickelacycle **8** and organometallic compounds (**R**-**M**) proceeds to give bis-homoallylic alcohol derivatives **9** (Scheme 2a) or homoallylic alcohols **10** (Scheme 2b) depending on the substrate structure, class of organometallic reagent, and type of ligand employed. We envisaged that, if a heterobimetallic compound, such as silylborane,[1e,h] is employed for the diene–aldehyde coupling, the reaction of oxanickelacycle **8** and the silylborane would proceed by a highly oxophilic boron atom interacting with an oxygen atom, giving the coupling product **11** through three different bond forming reactions (C–C, C–Si, and O–B) in one pot. We also expected that the coupling reaction would provide a new method for the synthesis of α-chiral allylsilanes.[11] Herein, we describe a novel three-component coupling of 1,3-dienes and aldehydes with commercially available (dimethylphenylsilyl)pinacolatoboron ($PhMe_2SiB(pin)$, **12**)[12] and its development into an enantio-



Scheme 2. Nickel-catalyzed coupling of 1,3-dienes and aldehydes via an oxanickelacycle intermediate. pin = pinacolato.

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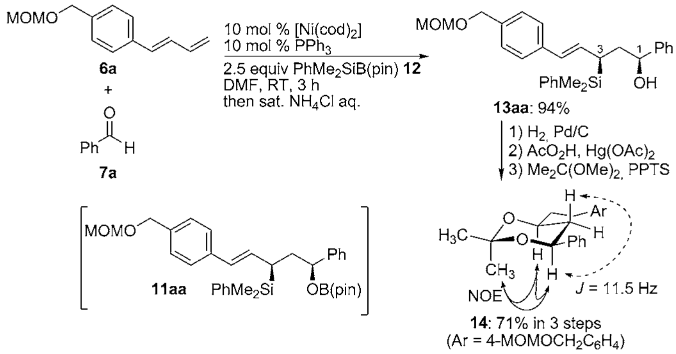
selective reaction,[13] leading to enantioenriched α-chiral allylsilanes.

To study the feasibility of a three-component coupling of 1,3-dienes, aldehydes, and a silylborane, we first investigated the reaction using achiral ligands. Thus, the reaction of 1,3-diene **6a**, benzaldehyde (**7a**), and $PhMe_2SiB(pin)$ (**12**) was carried out in the presence of 10 mol% of $[Ni(cod)_2]$ and 10 mol% of PPh_3 in DMF at room temperature for 3 hours (Scheme 3). As a result, the coupling product **13aa** was obtained in 94% yield as a single diastereomer. The relative stereochemistries of the hydroxy group at the C1 position and the $PhMe_2Si$ group at the C3 position of **13aa** were determined by ^1H NMR spectroscopy and NOESY experiments on **14** (derived from **13aa**) to be 1,3-*syn* orientation. This result indicated that the reaction of oxanickelacycle **8** with silylborane **12** proceeded to give the cross-coupling product **11aa** exclusively, as expected, from which **13aa** was produced by hydrolysis of the boron–oxygen bond.[14]

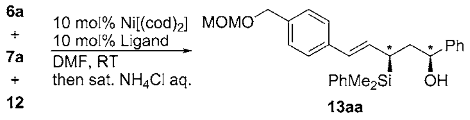


Scheme 3. Three-component coupling of 1,3-diene **6a**, benzaldehyde (**2a**), and silylborane **12** and determination of product stereochemistry at C1 and C3. cod = 1,5-cyclooctadiene, pin = pinacolato, MOM = methoxymethyl, PPTS = pyridinium *p*-toluenesulfonate.

Encouraged by this result, we set out to conduct a screen of various chiral ligands for the realization of an enantioselective version of the 1,3-diene and aldehyde coupling (Table 1). The coupling reaction of **6a**, **7a**, and **12** using chiral phosphine ligands, (*R*)-BnO-MOP,[15a] NMDPP, (*R*,*R*)-**15**,[15b] or phosphoroamidite ligand (*R*,*R*)-**16**,[15c] gave **13aa** in moderate yield and low *ee* (entries 1–4). However, the use of (*R*)-MonoPhos provided **13aa** in 70% yield, although the enantioselectivity was still low (entry 5). Based on these results, MonoPhos seemed to be a good starting point, so we decided to modify it and apply its analogues to the coupling reaction (entries 6–11). When *N*,*N*-diisopropyl and *N*,*N*-dibenzyl analogues (*R*)-**17a** and (*R*)-**17b**[15d] were employed, both the yield and *ee* of **13aa** decreased (entries 6 and 7). On the other hand, modification of the 3,3′ positions of the binaphthyl skeleton was found to be effective for improving the enantioselectivity (entries 8–12). Introduction of a methyl group ((*R*)-**17c**)[15d] and a phenyl group ((*R*)-**17d**)[15d] at the 3,3′-positions increased the *ee* of **13aa** to 52% and 58%, respectively (entries 8 and 9). The reaction using 3,3′-dimesityl derivative (*R*)-**17e** provided the coupling product **13aa** in 57% yield and 94% *ee* (entry 10). The coupling reaction using 3,3′-bis(diphenylmethyl) analogue (*R*)-**17f** gave **13aa** in 71% yield and 81% *ee* (entry 11). Finally, (*R*)-**17g**[15e] was found to be the most effective ligand, with **13aa** being produced in 71% yield and 97% *ee* (entry 12).[16]

With optimized conditions in hand, we explored the scope of the enantioselective coupling (Table 2). Reaction of **6a** with **7b** and **7c**, bearing an electron-donating group on the aromatic ring, afforded the corresponding products **13ab** and **13ac** in high yield and enantiopurity (entries 1 and 2). When 1,3-diene **6a** was reacted with *p*-trifluorobenzaldehyde (**7d**), the yield of **13ad** decreased to 29%, although the *ee* remained high (entry 3). Coupling reactions of bicyclic aromatic aldehydes **7e** and **7f** with **6a** also proceeded to afford the corresponding products **13ae** and **13af** in high yield and enantiopurity (entries 4 and 5). Aliphatic aldehydes **7g**–**7i** were also suitable for coupling with **6a**, giving allylsilanes **13ag**–**13ai** in a highly enantioselective manner (entries 6–8). The coupling of siladiene **6b** with **7a** gave **13ba** in 80% yield and 82% *ee* (entry 9). Also, alkyl substituted diene **6c** was coupled with **7a** and the corresponding product **13ca** was obtained in moderate yield and enantiopurity as a single diastereomer (entry 10). Next, the asymmetric coupling reaction of internal dienes with **7a** was investigated (entries 11 and 12). When the reaction of unsymmetrical diene **6d** and **7a** was carried out under optimized conditions, the corresponding coupling product **13da** was obtained in

Table 1: Screening of chiral ligands.[a]



Entry	Ligand	*t* [h]	Yield [%]	*ee* [%]
1	(*R*)-BnO-MOP	24	54	12[b]
2	NMDPP	3	57	1[b]
3	(*R*,*R*)-**15**	24	26	6[b]
4	(*R*,*R*)-**16**	16	37	2[b]
5	(*R*)-MonoPhos	24	70	−19[c]
6	(*R*)-**17a** (R^1 = H, R^2 = *i*Pr)	26	29	−4[c]
7	(*R*)-**17b** (R^1 = H, R^2 = Bn)	18	51	−9[c]
8	(*R*)-**17c** (R^1 = R^2 = Me)	13	56	−52[c]
9	(*R*)-**17d** (R^1 = Ph, R^2 = Me)	18	59	−58[c]
10	(*R*)-**17e** (R^1 = mesityl, R^2 = Me)	26	57	94[b]
11	(*R*)-**17f** (R^1 = $CHPh_2$, R^2 = Me)	24	71	81[b]
12	(*R*)-**17g** (R^1 = $CHPh_2$, R^2 = Bn)	22	71	97[b]

[a] cod = 1,5-cyclooctadiene, MOM = methoxymethyl. [b] (1*S*,3*R*)-**13aa** was formed as the major enantiomer. [c] (1*R*,3*S*)-**13aa** was formed as the major enantiomer. The absolute configuration of **13aa** was determined by transformation to a known compound. For details, see the Supporting Information.

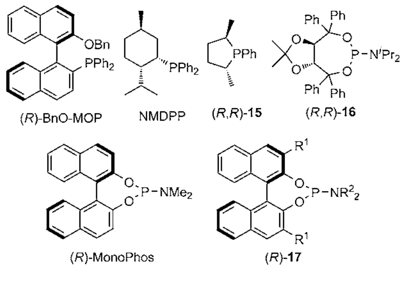
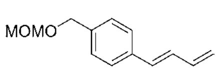
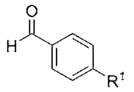
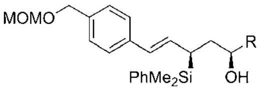
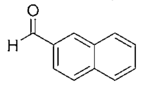
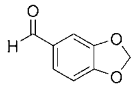
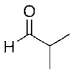
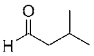
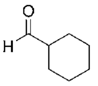
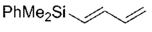
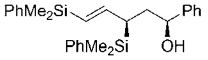
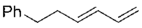
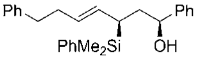
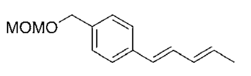
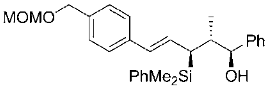
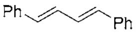
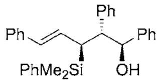


Table 2: Asymmetric coupling of various dienes and aldehydes with silylborane **12**.[a]

Entry	Diene	Aldehyde	Product: yield, *ee* (*t*)
			
1	**6a**	**7b**: R^1 = Me	**13ab**: 89%, 96% *ee* (20 h)
2		**7c**: R^1 = OMe	**13ac**: 92%, 92% *ee* (5 h)
3		**7d**: R^1 = CF$_3$	**13ad**: 29%, 85% *ee* (48 h)
4		 **7e**	**13ae**: 72%, 92% *ee* (24 h)
5		 **7f**	**13af**: 82%, 92% *ee* (18 h)
6		 **7g**	**13ag**: 68%, 96% *ee* (18 h)
7		 **7h**	**13ah**: 56%, 97% *ee* (20 h)
8		 **7i**	**13ai**: 74%, 94% *ee* (18 h)
9	 **6b**	**7a**	 **13ba**: 80%, 82% *ee* (36 h)
10	 **6c**	**7a**	 **13ca**: 62%, 66% *ee* (17 h)
11	 **6d**	**7a**	 **13da**: 22%, 92% *ee* (40 h)
12	 **6e**	**7a**	 **13ea**: 51%, 20% *ee* (48 h)

[a] Reaction conditions: Diene **6** (1 equiv), aldehyde **7** (2.5 equiv), [Ni(cod)$_2$] (10 mol%), (*R*)-**17g** (10 mol%), PhMe$_2$SiB(pin) (**12**, 2.5 equiv), DMF, RT.

22% yield and 92% *ee* (entry 11). When (*E*,*E*)-1,4-diphenylbuta-1,3-diene (**6e**) was employed for the coupling with **7a** and **12**, **13ea** was produced in 51% yield and 20% *ee* as a single diastereomer (entry 12).

In summary, we have succeeded in developing an enantio- and diastereoselective three-component coupling of 1,3-dienes, aldehydes, and a silylborane. This coupling reaction is the first example of an asymmetric coupling of two different types of unsaturated compounds with a bimetallic reagent and represents a new synthetic approach to optically active α-chiral allylsilane derivatives. Further studies, including a mechanistic investigation, are in progress.

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Keywords: aldehydes · asymmetric catalysis · dienes · nickel · silylborane

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