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LETTERS

Development of Zinc Borates Designed for Functionalized Hard Nucleophiles in the Coupling Reaction with Allylic Alcohol Derivatives

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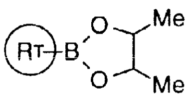
Abstract: Zinc borates **3** (R^T = aryl, alkenyl), prepared from the boronate esters **1** and MeZnCl, were developed for the title reaction. Thus, reaction of the allylic acetates **6a–c** with the aryl borates **3a–f** and the alkenyl borates **3g,h** in the presence of $NiCl_2(PPh_3)_2$ (10 mol%) and DMI (10 equiv) at 40–50 °C afforded the coupling products **8a–o** in good yields (Tables 1 and 2). Since MeZnCl is almost inert toward carbonyl groups, this method is applicable for the functionalized borates **3**.

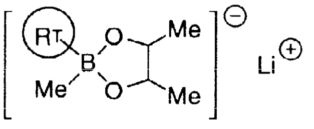
Key words: allylation; boron and compounds; coupling reactions; zinc and compounds

In the last two decades, organometallics based on boron,[1] tin,[2] and zinc[3] have been utilized as reagents for the transition metal-catalyzed coupling reaction. These reagents participate well in the coupling with aryl and alkenyl substrates. However, the boron and tin reagents, which are prepared by several methods, suffer from low reactivity toward allylic substrates because of the stable nature of the carbon-metal bond.[1,2,4,5] On the other hand, the zinc reagents possessing a carbonyl group can not be prepared since the classical lithium or magnesium reagents, which generally show high nucleophilicity toward the carbonyl groups, are used as precursors.[3] With these limitations unsolved, much attention has recently been focused on preparation of functionalized organozincs, for which independent works by Knochel, Tamaru, and Reike are well known.[6-10] So far, the reactivities of these organozincs toward aryl and alkenyl substrates have been demonstrated to be almost the same as those prepared using the classical reagents.[11] However, the allylic coupling is awkward. An attempt by Tamaru resulted in the homocoupling.[12] Therefore, transmetalation to more reactive copper reagents is required to achieve allylic coupling successfully.[11,13,14] Even then, allylic partners are limited to allylic halides, which are known to be the most reactive substrates among allylic compounds. On the basis of availability and synthetic application, allylic alcohol derivatives, especially secondary ones, are definitely desirable partners.

Recently, we reported the high reactivity of the lithium borates **2** toward allylic alcohol derivatives.[15] In addition to the higher reactivity, the neutral nature gifted with **2** expands the scope of allylic substrates to those possessing ester and hydroxyl groups. We used MeLi for preparation of **2** from the boronate esters **1**. Thus, finding an organometallic which attacks the central boron atom faster than a functional group present in the boronate ester should directly lead to an alternative method for functionalized hard nucleophiles which are effective

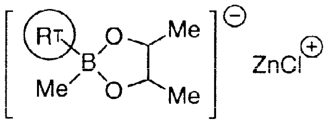


1



2

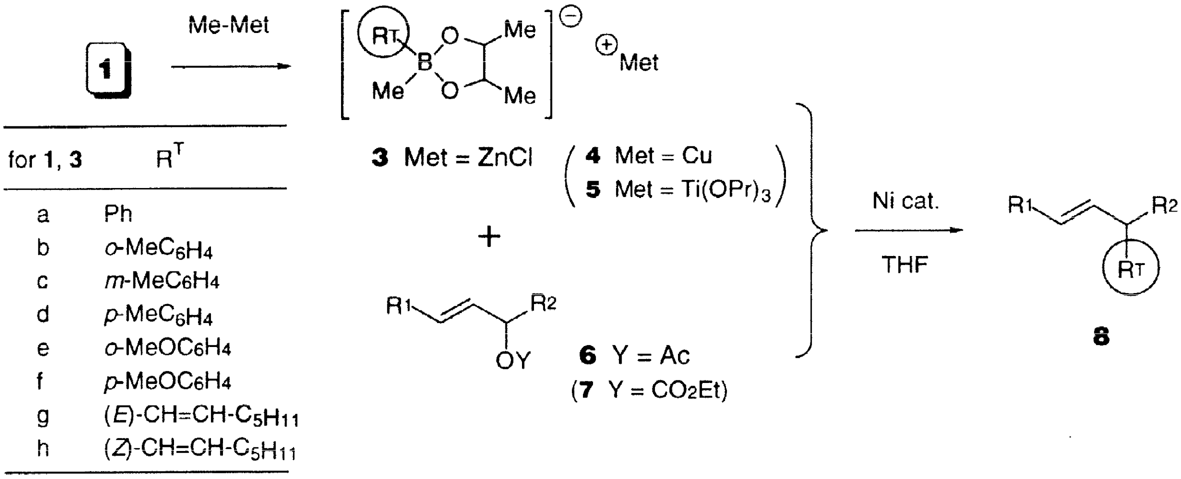
previou reeagents



3

present reagents

PII: S0040-4039(98)01638-4



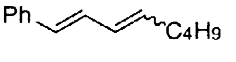
for **1**, **3**	R^T
a	Ph
b	*o*-MeC_6H_4
c	*m*-MeC_6H_4
d	*p*-MeC_6H_4
e	*o*-$MeOC_6H_4$
f	*p*-$MeOC_6H_4$
g	(*E*)-CH=CH-C_5H_{11}
h	(*Z*)-CH=CH-C_5H_{11}

Scheme 1

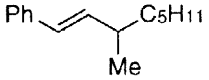
for the coupling with allylic alcohol derivatives. We found that MeZnCl is the reagent of choice. Herein we report reactivity of the new coupling reagents, zinc borates **3**, toward the coupling reaction with secondary allylic substrates. In the following letter, preparation of functionalized zinc borates possessing various carbonyl groups and their coupling reaction are described.

Initially, three methyl-metals, MeZnCl, MeCu, and MeTi(O-*i*-Pr)$_3$ were selected for the study on the basis of the low nucleophilicity toward carbonyl groups,[16] while the phenylboronate ester **1a** (R^T = Ph) was chosen as a representative precursor of the borate. Conversion of **1a** to the corresponding borate using the above methyl-metal was studied in THF between 0 °C and room temperature for 0.5–4 h and the supposed borate, without isolation, was submitted to the coupling with the secondary allylic substrates **6a** and **7a** (R^1 = Ph, R^2 = *n*-C_5H_{11}) in the presence of 10 mol% of $NiCl_2(PPh_3)_2$ or $NiCl_2$(dppf) at or above room temperature overnight (Scheme 1).

Among the methyl-metals, MeZnCl afforded the coupling product **8a** (R^T = R^1 = Ph, R^2 = *n*-C_5H_{11}), while MeCu and MeTi(O-*i*-Pr)$_3$ were less effective and acetate **6a** was recovered quantitatively. In contrast to the reaction of MeCu and organoboranes where the dummy ligand is an alkyl group,[17] MeCu did not produce the borates from **1a**. Results obtained with MeZnCl under various conditions are summarized in Table 1. Throughout the preliminary investigation, acetate **6a** was slightly more reactive than carbonate **7a**. As for the nickel complexes, $NiCl_2(PPh_3)_2$ and $NiCl_2$(dppf) both showed similar potency as a catalyst (entries 1,2,8,9). A reaction time of 30 min at room temperature was enough for preparation of the zinc borate **3a** and the coupling was completed within 12 h under a slightly higher temperature of 40–50 °C (cf. entry 3). Neither the regioisomer nor *cis* isomer was detected by ^{1}H NMR (300 MHz) spectroscopy. Although the diene **9** and the methyl-coupling product **10** were produced as by-products (2–9% each) in most cases, their production was suppressed to less than 2% combined yield by addition of 1,3-dimethyl-2-imidazolidinone (DMI) or *N*,*N*-dimethyl formamide (DMF) (entries 6 and 7) and such by-products, if any, were easily separated by silica gel chromatography. Use of Et_2Zn and *n*-BuZnCl in place of MeZnCl was unsuccessful (data not shown). Palladium complexes such as $PdCl_2(PPh_3)_2$, $Pd(PPh_3)_4$ were totally ineffective for the present coupling.



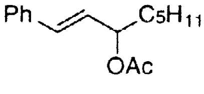
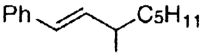
9



10

Before going to functionalized borates, efficiency of the zinc borate-method was briefly examined and the results are delineated in Table 2. Reactions of the Me- or MeO-substituted aryl boronate esters **1b–f** with MeZnCl and the subsequent couplings with **6a** in the presence of $NiCl_2(PPh_3)_2$ (5-10 mol%) and DMI (10 equiv) proceeded

Table 1. Coupling Reaction of Allylic Substrates 6a,7a (R^1 = Ph, R^2 = n-C_5H_{11}) and Zinc Borate 3a (R^T = Ph)[a]

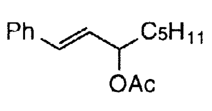
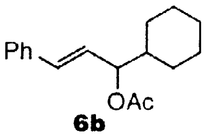
run	substrate	cat.[b]	polar solvent[c]	temp.(°°C)	yield (%) of **8a**[d,e]	ratio[f] of **8a** : **9** : **10**
1	 **6a**	$NiCl_2(PPh_3)_2$	-	40–50	88	91 : 5 : 4
2		$NiCl_2$(dppf)	-	40–50	81	91 : 3 : 6
3		$NiCl_2(PPh_3)_2$	-	rt	85	87 : 4 : 9
4		$NiCl_2(PPh_3)_2$	MeCN	40–50	78	89 : 6 : 5
5		$NiCl_2(PPh_3)_2$	DMSO	40–50	83	89 : 6 : 5
6		$NiCl_2(PPh_3)_2$	DMI	40–50	87	-----------[g]
7		$NiCl_2(PPh_3)_2$	DMF	40–50	80	-----------[g]
8	 **7a**	$NiCl_2(PPh_3)_2$	-	40–50	88	92 : 4 : 4
9		$NiCl_2$(dppf)	-	40–50	84	90 : 2 : 8

[a] Prepared from **1a** and MeZnCl in THF. [b] 10 mol%. [c] Added 10 equiv in a THF solution. [d] R^1 = R^T = Ph, R^2 = n-C_5H_{11}. [e] Isolated yield by chromatography. [f] Determined by ^1H NMR (300 MHz) spectroscopy. [g] Neither **9** nor **10** was detected by ^1H NMR.

exclusively to furnish **8b–f** in good yields regardless of the substituent pattern on the aromatic ring (entries 1–5).[18,19] The excellent reactivity did not put any restriction on allylic acetates. Acetates with a different size of substituent (i.e., **6b,c**) reacted with borates **3a,b,f** efficiently (entries 8–10,12,13). Noteworthy is the fact that the sterically hindered boronate esters **1b,1e** are converted into borates **3b,3e** and that, more importantly, these borates keep high reactivity toward acetate **6a** and the more bulky acetate **6b** (entries 1,4,9). Finally, alkenyl reagents were also examined to confirm that the coupling proceeds with similar efficiency and without double bond isomerization (entries 6,7,11).

In conclusion, we have presented the zinc borates **3** which work as hard nucleophiles in the coupling with

Table 2. Nickel-Catalyzed Coupling Reaction of Allylic Acetates 6a-c and Zinc Borates 3a–h in the Presence of DMI[a]

run	acetate	borate[b,c]	**8**[d]	yield(%)[e]	run	acetate	borate[b,c]	**8**[d]	yield(%)[e]
1	 **6a**	**3b**	**8b**	89	8	 **6b**	**3a**	**8i**	94
2		**3c**	**8c**	81	9		**3b**	**8j**	82
3		**3d**	**8d**	87	10		**3f**	**8k**	98
4[f]		**3e**	**8e**	88	11		**3g**	**8l**	81
5		**3f**	**8f**	76					
6		**3g**	**8g**	85	12	 **6c**	**3a**	**8n**	95
7		**3h**	**8h**	77	13[f]		**3f**	**8o**	91

[a] Reactions were carried out in the presence of $NiCl_2(PPh_3)_2$ (5–10 mol%) and DMI (10 equiv) between 40-50 °C in THF overnight. [b] R^T: see Scheme 1. [c] Prepared from the corresponding boronate esters and MeZnCl in THF. [d] R^1, R^2, and R^T are the same as those of **6a–c** and **3a–h**. [e] Combined yields of the by-products (the diene and the Me–coupling product) were <2% by ^1H NMR spectroscopy. [f] Carried out without DMI.

allylic alcohol derivatives. Since a separate experiment confirmed that MeZnCl is unreactive toward the aldehyde under similar conditions used for the generation of **3** from **1**,[16] it is evident that the present procedure is applicable to the boronate esters possessing carbonyl groups and these results are described in the following letter.[20]

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19. Lower product-selectivity was observed when DMF was used as the co-solvent in the reaction of **3b** and **6a**.
20. This paper is dedicated to Professor Sigeru Torii in commemoration of his retirement from Okayama University.