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LETTERS

Preparation of Functionalized Zinc Borates and their Coupling Reaction with Allylic Acetates

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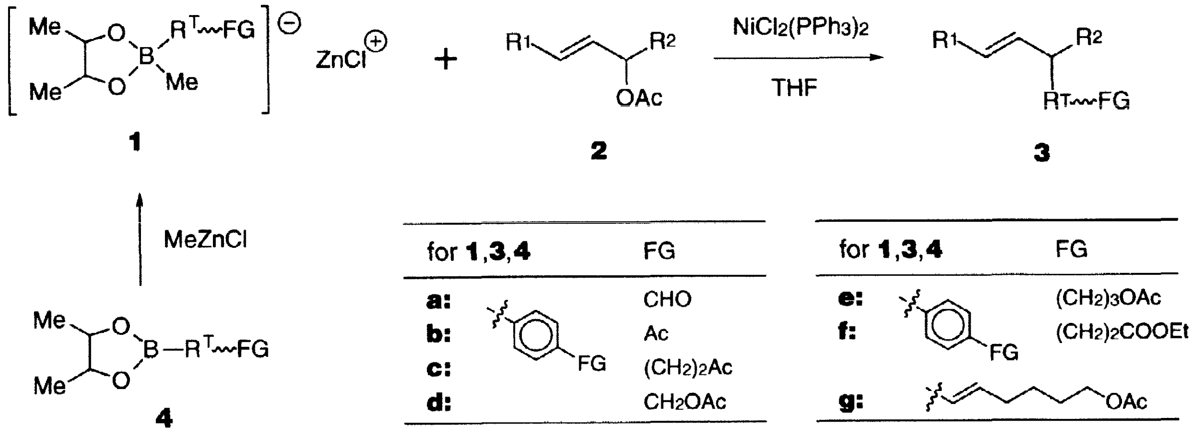
Abstract: Several methods were examined to prepare functionalized boronate esters **4a–g**. Thus, reaction of the lithium anions with $B(O\text{-}i\text{-}Pr)_3$ followed by esterification with 2,3-butanediol afforded **4a,b,d,e**. The Masamune-Wittig reaction was applied to the boronate ester **4a** to expand the carbon chain giving **4c** and **4f**. The alkenyl boronate ester **4g** was prepared from acetylene **10** by hydroboration using $(Ipc)_2BH$ followed by the ligand exchange reaction. © 1998 Elsevier Science Ltd. All rights reserved.

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

Protection of reactive functional group(s) on the nucleophilic reagents is a general protocol to avoid unwanted side reaction(s). Thus, finding a reagent with a wide range of functional group compatibility not only provides a efficient tool for organic synthesis, but also can avoid troublesome protection and deprotection steps. Recently, much attention has been focused on preparation of functionalized organozincs.[1] In contrast to the transition metal-catalyzed coupling with aryl- and alkenyl halides and their synthetic equivalents, these reagents show quite lower reactivity in the allylic coupling even with the allylic halides, the most reactive substrates among the allylic substrates. In the preceding letter, we have prepared the zinc borates **1** (R^T–FG = Ar) from the boronate esters **4** and MeZnCl and shown the coupling reaction with allylic acetates **2** in the presence of a nickel catalyst (Scheme 1).[2] Since MeZnCl are marginally reactive toward the aldehyde examined,[3] this method should provide a chance to realize, for the first time, the allylic coupling with hard nucleophiles possessing a carbonyl group,[4] though it



Scheme 1

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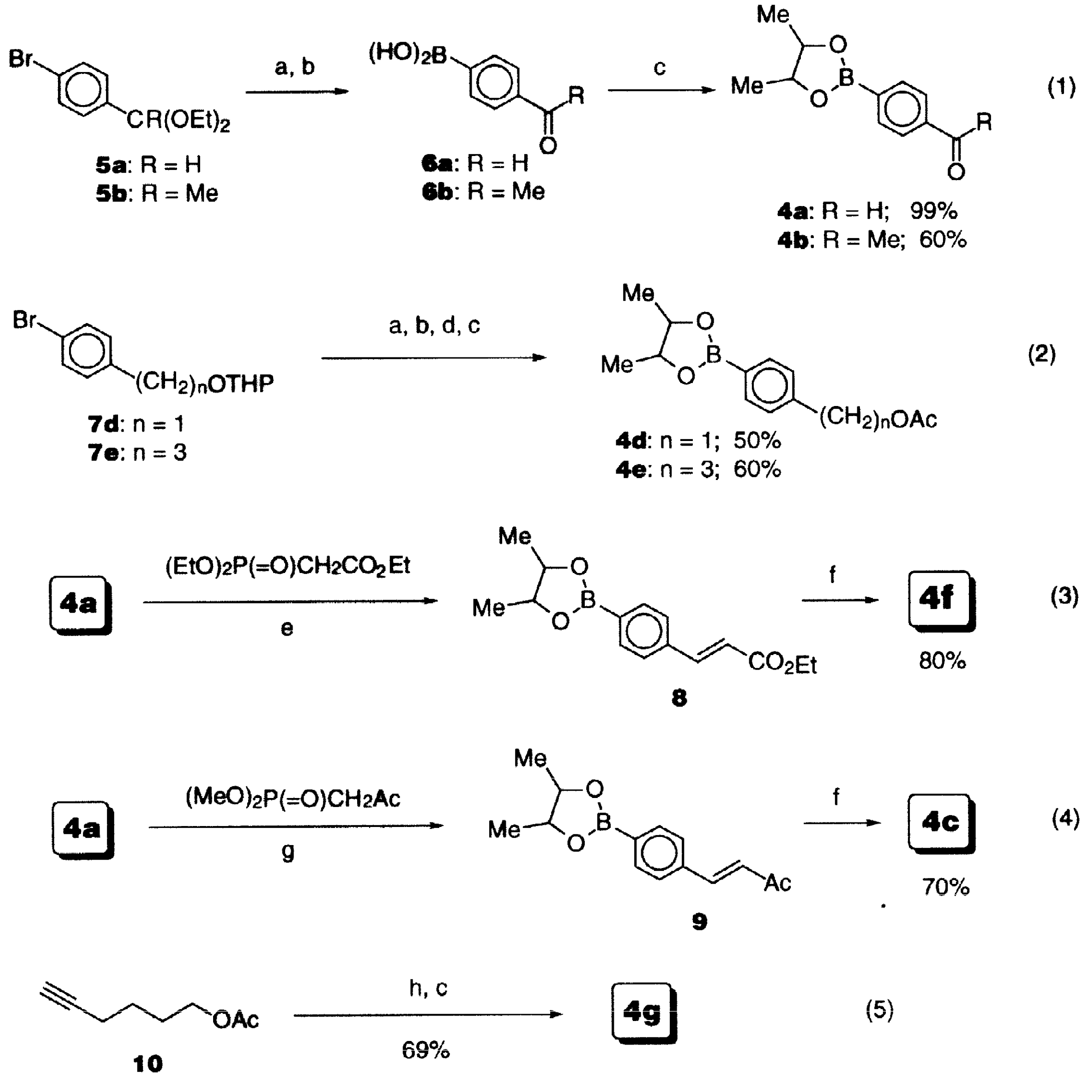
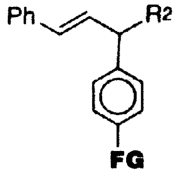


Scheme 2. Preparation of the Boronate Esters 4a–4g: [a] n-BuLi, –78 °C then B(O-i-Pr)$_3$; [b] H_3O^+; [c] 2,3-butanediol, $MgSO_4$; [d] Ac_2O, C_5H_5N; [e] $(EtO)_2P(=O)CH_2CO_2Et$, LiCl, DBU; [f] H_2, Pd/C; [g] $(MeO)_2P(=O)CH_2Ac$, LiCl, i-Pr_2NEt; [h] $(Ipc)_2BH$ then MeCHO.

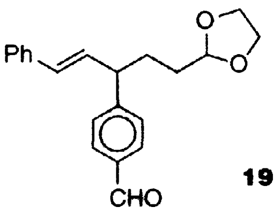
was not clear whether the electron withdrawing nature of a carbonyl group directly attached to the aromatic ring of the borates decrease the coupling reactivity. Herein we report preparation of the boronate esters **4** incorporating an aldehyde-, ketone-, or ester-group and their reaction with allylic acetates. During this investigation, we found that the Masamune-Witting reaction is applicable to an aldehyde in which the boronate ester-group is already incorporated.

Several methods were examined to obtain the aryl- and alkenylboronate esters **4** and the successful results are summarized in Scheme 2. Intuitively one might think that the boronate ester-group should be introduced at the final stage of the sequence due to its high reactivity toward nucleophiles as is shown in the previous paper. This was, in fact, the situation and **4a,b,d,e** were prepared efficiently, keeping the high reactivity toward nucleophiles in mind, by using the literature method[5] (generation of the lithium anions followed by reaction with B(O-i-Pr)$_3$ to instal the boron atom on the molecules). Since the method giving aldehyde **4a** in large quantity is established, we explored the reverse possibility. After several trials, the modified Wittig-Horner reaction reported by Masamune[6]

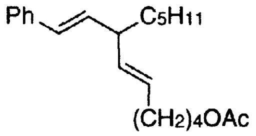


11–18

product	R^2	FG	yield,%
11	n-C_5H_{11}	CHO	75
12	c-C_6H_{11}	CHO	89
13	n-C_5H_{11}	Ac	87
14	n-C_5H_{11}	CH_2OAc	89
15	n-C_5H_{11}	$(CH_2)_3OAc$	83
16	c-C_6H_{11}	$(CH_2)_3OAc$	92
17	n-C_5H_{11}	$(CH_2)_2CO2Et$	88
18	c-C_6H_{11}	$(CH_2)_2Ac$	85



19 70%



20 87%

Chart 1

was found to be applicable to aldehyde **4a**. To the best of our knowledge, this is a rare case of an anionic carbon-carbon bond forming reaction on a reactive boron-containing substrate.[7] For preparation of the alkenyl boronate ester **4g**, the method of Suzuki and Miyaura[8] was found to be more efficient than others which are based on catecholborane,[9] pinacolborane,[10] or 2,3-butanediol-borane.[11]

With the above functionalized boronate esters in hand, coupling reactions with allylic acetates were carried out under the conditions described above (Scheme 1) and results are summarized in Chart 1. In all the cases, MeZnCl attacked the boron atom on the boronate esters selectively to form the corresponding borates **1** which, upon reaction with the acetates, afforded coupling products **11–20** in high yields. Among them, the results obtained with the boronate ester **4a** are noteworthy in that: (1) the borate **1a** was indeed generated cleanly without attack on the aldehyde-carbon; (2) the electron-withdrawing nature of the aldehyde-group did not affect the reactivity, thus giving **11**,**12**, and **19** in good yields without any by-product(s). In addition to this, synthesis of **19** demonstrates the efficiency of the present methodology since two aldehyde-groups on **19** are differentiated.

In conclusion, we have presented the first example of functionalized hard nucleophiles for the coupling reaction using allylic alcohol derivatives. The designed zinc borates are highly reactive so that installation of aryl and alkenyl groups possessing an aldehyde, ketone, and/or ester-group is easily achieved even to a sterically congested *sec*-allylic position. Extension of the zinc borate chemistry to other types of catalytic reactions is now under investigation.

Preparation of the Boronate Ester 4f: A mixture of **4a** (204 mg, 1.0 mmol), LiCl (51 mg, 1.2 mmol), $(EtO)_2P(=O)CH_2CO_2Et$ (0.24 mL, 1.2 mmol), and DBU (0.18 mL, 1.2 mmol) in MeCN (4 mL) was stirred at room temperature overnight and filtered through a pad of silica gel. The filtrate was concentrated to afford the crude product **8**, which was then dissolved in EtOH (10 mL). After addition of 10% Pd/ C (108 mg), the mixture was flushed with hydrogen, stirred at room temperature overnight, and filtered through a pad of Celite. The filtrate was concentrated and the residue was purified by chromatography on silica gel to furnish **4f** (221 mg, 80%

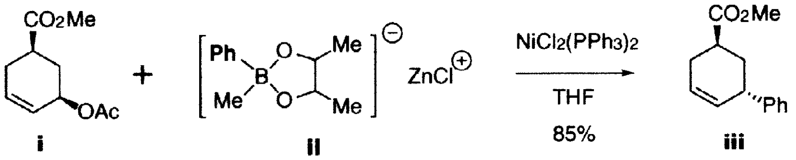
yield).

General Procedure for the Coupling Reaction: To an ice-cold solution of anhydrous $ZnCl_2$ (123 mg, 0.90 mmol) in THF (5 mL) was added MeLi in Et_2O (0.62 mL, 1.46 M, 0.90 mmol). The cooling bath was removed and the resulting solution was stirred at room temperature for 30 min to prepare a MeZnCl solution. The boronate ester **4a** (193 mg, 0.95 mmol) was added to the solution and, after 30 min of stirring at room temperature, the allylic acetate **2** (R^1 = Ph, R^2 = c-C_6H_{11}) (78 mg, 0.30 mmol) and $NiCl_2(PPh_3)_2$ (20 mg, 0.03 mmol) were added. The mixture was stirred overnight at between 40 and 45 °C and poured into a mixture of hexane and sat. NH_4Cl solution with vigorous stirring. The organic layer was separated and the aqueous layer was extracted with hexane. The combined hexane layers were dried ($MgSO_4$) and concentrated to give an oil, which was purified by chromatography on silica gel to afford the coupling product **12** (81 mg, 89%).[12]

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture, Government of Japan.

REFERENCES AND NOTES

1. See ref. 6–10 of the preceding paper.
2. The stereochemical aspect of the reaction was examined by using cyclic acetate **i**[2a] and the zinc borate **ii**. Stereochemistry of the product obtained in high yield was assigned to be *trans* as is depicted in **iii** by comparison with the reported data.[2b] This result indicates that the present reaction proceeds with the widely accepted mechanism for the hard nucleophiles and involves formation of the π-allylnickel inter-mediates followed by the transmetalation with the zinc borates and the subsequent reductive elimination. (a) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4730-4743. (b) Sheffy, F. K.; Godschalx, J. P.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4833-4840.



3. See ref. 16 of the preceding paper.
4. Earlier attempt of this type of reaction: see ref. 12 of the preceding paper.
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6. Blanchette, M. A.; Choy, W.; Davis, J. T.; Essenfeld, A. P.; Masamune, S.; Roush, W. R.; Sakai, T. *Tetrahedron Lett.* **1984**, *25*, 2183-2186.
7. Difference in the reaction site between MeZnCl and the phosphonate anions (boron atom vs aldehyde carbon) is understandable on the basis of the thermodynamic (for anion derived from the phosphonates) and kinetic (for MeZnCl) nature of the reactions. Substitution reaction of compounds which possess a sterically hindered and thence more stable pinacol boronate ester-group is reported in ref. 8.
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11. Unpublished result.
12. This paper is dedicated to Professor Sigeru Torii in commemoration of his retirement from Okayama University.