Cross-Coupling

DOI: 10.1002/ange.201103601

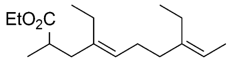
Highly Regio- and Stereoselective Synthesis of Multialkylated Olefins through Carbozirconation of Alkynylboronates and Sequential Negishi and Suzuki–Miyaura Coupling Reactions**

Yasushi Nishihara, Yoshiaki Okada, Jiao Jiao, Masato Suetsugu, Ming-Tzu Lan, Megumi Kinoshita, Masayuki Iwasaki, and Kentaro Takagi*

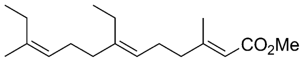
Dedicated to Professor Tamejiro Hiyama on the occasion of his 65th birthday

The regio- and stereoselective synthesis of multisubstituted olefins is one of the most challenging tasks in synthetic organic chemistry.[1] Established synthetic methods to directly construct carbon–carbon double bonds, such as Wittig, Horner–Wadsworth–Emmons, or olefin metathesis have limitations and often afford inseparable mixtures of stereoisomers. Recent advances in carbometalation or bimetalation/cross-coupling strategies have provided a facile entry to multisubstituted olefins, albeit often with problematic regio- and stereoselectivities.[2] Although efficient multicomponent coupling reactions have been used to achieve the synthesis of multisubstituted olefins bearing aromatic substituents,[3] a general approach to multialkylated olefins has yet to be defined.[4]

Aliphatic multialkylated olefins are common motif in natural products and occur, for example, in various insect sex pheromones and hormones.[5] In addition to their importance in nature, multialkylated olefins are often used as key intermediates in the synthesis of other compounds. For example, the diene **I** is a precursor of the antibiotic lasalocid A,[6] and triene **II** is the final intermediate in a synthesis of Cecropia juvenile hormone.[7]

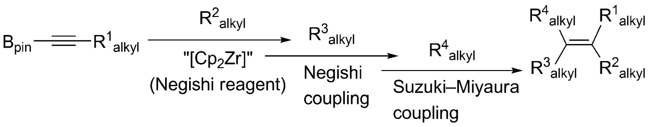


I



II

Although the simple textbook approach to multialkylated olefins would be an elimination reaction (e.g. E2 reaction), neither Hofmann (less-substituted olefins)[8] nor Saytzeff (more-substituted olefins)[9] elimination can perfectly control reaction selectivity with mixtures of structural isomers being obtained. Recently, our research group has demonstrated the usefulness of 1-alkynylboronates[10] and 1-alkynylsilanes[11] as applied to zirconium chemistry to afford a highly regio- and stereoselective syntheses of multisubstituted olefins. Herein, we describe a practical and versatile procedure for the formation of tri- and tetrasubstituted olefins bearing different β-hydrogen-containing alkyl groups by carbozirconation of 1-alkynylboronates and successive Negishi[12] and/or Suzuki–Miyaura[13] cross-coupling reactions with high regio- and stereoselectivities (Scheme 1).



Scheme 1. Synthetic concept. $\mathrm{B_{pin}}$ = pinacolatoboryl, Cp = cyclopentadienyl.

Addition of 1-alkynylboronates **1a**–**1e**[14] to Negishi reagent ($[\mathrm{Cp_2ZrCl_2}]/2\,n\mathrm{BuLi}$)[15] generated in situ under an atmosphere of ethylene smoothly produced zirconacyclopentenes[16] which, upon hydrolysis, afforded the corresponding alkenylboronates **2a**–**2e** in moderate to high yields with excellent regioselectivity [Eq. (1)].[17] The regiochemistry of **2a**–**2e** was confirmed by comparison of their spectroscopic data with those reported for authentic compounds[18] prepared by the reactions of 1-alkynylboronates with Takahashi reagent ($[\mathrm{Cp_2ZrCl_2}]/2\,\mathrm{EtMgBr}$),[19] as well as ^{1}H NMR spectra that show the presence of a highly shifted triplet with a small coupling constants ($J = 1.5$ Hz) in the double bond region (5.02–5.13 ppm), and is indicative of a hydrogen atom located geminal to the boron functionality. Alternately, the $^{11}\mathrm{B}\{^1\mathrm{H}\}$ NMR chemical shift of **2a** (29.9 ppm) is characteristic of vinylboronates.

With the regiocontrolled alkenylboronates **2a** in hand, we pursued the Suzuki–Miyaura coupling of alkenylboronates with alkyl bromides. In general, organoboronates are relatively inert compounds compared to the corresponding

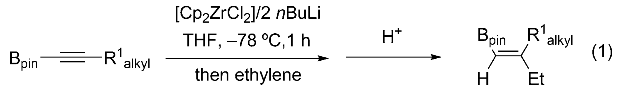
---

[*] Prof. Dr. Y. Nishihara, Y. Okada, J. Jiao, M. Suetsugu, M.-T. Lan, M. Kinoshita, Prof. Dr. M. Iwasaki, Prof. Dr. K. Takagi
Division of Chemistry and Biochemistry, Graduate School of Natural Science and Technology, Okayama University
3-1-1 Tsushimanaka, Kita-ku, Okayama 700-8530 (Japan)
E-mail: ynishiha@cc.okayama-u.ac.jp

[**] We gratefully thank Prof. Hiroshi Nakazawa and Dr. Masumi Itazaki at Osaka City University for measurements of elemental analyses and Prof. Tamotsu Takahashi at Hokkaido University for generous donation of zirconocene dichloride. This work was supported by a Grant-in-Aid for Scientific Research on Priority Areas "Advanced Molecular Transformations of Carbon Resources" from the Ministry of Education, Culture, Sports, Science and Technology (Japan).

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201103601.

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



(1)

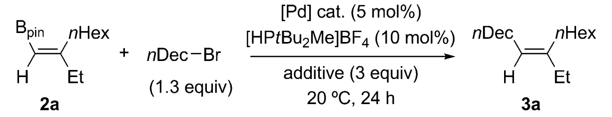
1a: R^1_{alkyl} = *n*Hex
1b: R^1_{alkyl}= *n*Dec
1c: R^1_{alkyl}= *n*Bu
1d: R^1_{alkyl} = *i*Pr
1e: R^1_{alkyl} = *t*Bu

2a: R^1_{alkyl} = *n*Hex; 81%
2b: R^1_{alkyl}= *n*Dec; 85%
2c: R^1_{alkyl} = *n*Bu; 58%
2d: R^1_{alkyl} = *i*Pr; 70%
2e: R^1_{alkyl} = *t*Bu; 81%

organoboronic acids.[20] Although it has been reported that the Suzuki–Miyaura coupling of alkenylboronates with alkyl bromides possessing β-hydrogen atoms proceed at 60 °C,[21] the higher temperature caused undesired β-hydrogen elimination in our previously reported nickel-catalyzed cross-coupling of alkenylboronates with alkyl iodides.[10] Thus, we screened various milder reaction conditions (Pd catalyst, additive, and solvent) and discovered that, under the basic conditions developed by Fu and co-workers,[22] wherein [HP*t*Bu$_2$Me]BF$_4$ is used as a precursor of the phosphine ligand, the reaction proceeded smoothly at room temperature.

As a test reaction, we chose to examine the cross-coupling of a β-hydrogen-containing alkyl bromide (1-bromodecane) with an alkenylboronate **2a** to yield **3a**. In this case, the conditions that Fu had found to be optimal for Suzuki–Miyaura coupling of alkyl bromides with arylboronic acids[22] were not optimal for the present reaction (Table 1, entry 1). We thus surveyed a broad range of conditions, and an illustrative subset of our findings is provided in Table 1. For example, we explored the use of Lewis base additives, and determined KOH to be the best (Table 1, entries 1–5). The choice of solvent had a significant impact on the efficiency of the reaction; use of THF rather than *tert*-amyl alcohol led to a marked enhancement in yield of **3a** (Table 1, entry 6). Use of [Pd(dba)$_2$], rather than Pd(OAc)$_2$ was beneficial and resulted in a slightly more effective coupling (Table 1, entry 7). Although [PdCp(π-allyl)] was found to be as effective as [Pd(dba)$_2$] (Table 1, entry 8), we chose to focus our study on [Pd(dba)$_2$]/KOH because of cost considerations. Increasing the reaction concentration delivered a quantitative yield of the product (Table 1, entry 9).

Table 1: Suzuki–Miyaura cross-coupling of 1-bromodecane with alkenylboronate **2a**.[a]

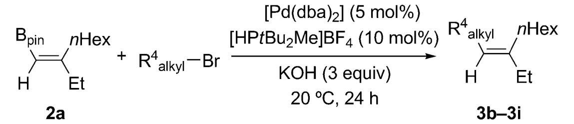


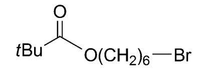
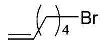
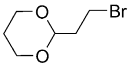
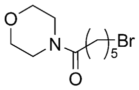
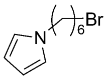
Entry	[Pd] cat.	Additive	Solvent	Yield [%][b]
1[c]	Pd(OAc)$_2$	KO*t*Bu	*tert*-amyl alcohol	47
2[d]	Pd(OAc)$_2$	KO*t*Bu	*tert*-amyl alcohol	32
3	Pd(OAc)$_2$	KOH	*tert*-amyl alcohol	63
4	Pd(OAc)$_2$	Ba(OH)$_2$	*tert*-amyl alcohol	<1
5	Pd(OAc)$_2$	CsF	*tert*-amyl alcohol	<1
6	Pd(OAc)$_2$	KOH	THF	81
7	[Pd(dba)$_2$]	KOH	THF	96
8	[PdCp(π-allyl)]	KOH	THF	91
9[e]	[Pd(dba)$_2$]	KOH	THF	99 (93)

[a] The reactions were carried out using **2a** (0.2 mmol), 1-bromodecane (0.26 mmol), and additive (0.6 mmol) in solvent (1 mL). [b] Determined by GC analysis of the crude reaction mixture. Yield of isolated product is shown in parenthesis. [c] Reaction carried out according to the procedure in Ref. [22]. [d] 6 equivalents of additive was used. [e] 0.5 mL of solvent was used. dba = dibenzylideneacetone, THF = tetrahydrofuran.

Using our optimized reaction conditions, we performed Suzuki–Miyaura cross-coupling of an array of β-hydrogen-containing alkyl bromides (Table 2). The process produced the desired cross-coupled products **3b**–**3i** in good to excellent yields and was compatible with variety of functional groups, including aryl, chloride, nitrile, ester, alkene, acetal, amide, and pyrrole (Table 2, entries 1–8). As a result of the mild reaction condition, no alkenes produced by β-hydrogen elimination were detected.

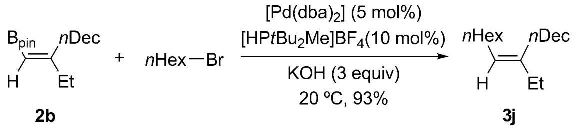
Table 2: Synthesis of trialkylated ethenes **3b**–**3i** by stereocontorolled Suzuki–Miyaura cross-coupling of alkenylboronate **2a** with alkyl bromides bearing β-hydrogen atoms.[a]



Entry	R^4_{alkyl}–Br	Product	Yield [%][b]
1	Ph(CH$_2$)$_3$–Br	**3b**	79
2	Cl(CH$_2$)$_6$–Br	**3c**	98
3	NC(CH$_2$)$_4$–Br	**3d**	64
4		**3e**	78
5		**3f**	78
6		**3g**	83
7		**3h**	81
8		**3i**	80

[a] The reactions were carried out using **2a** (1 mmol) and alkyl bromide (1.3 mmol) in THF (2.5 mL). [b] Yield of isolated product.

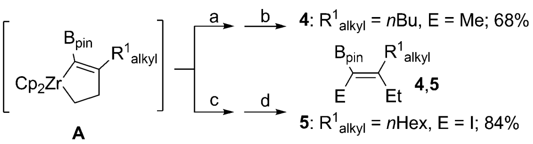
Notably, the regiochemistry of the cross-coupled product can be readily reversed by swapping the functionality on the alkyl group in alkynylboronates **1** and the alkyl bromide. For example, 1-alkynylboronate **2b** was successfully treated with 1-bromohexane to produce the cross-coupled product **3j**, which is a regioisomer of **3a** [Eq. (2)].



(2)

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

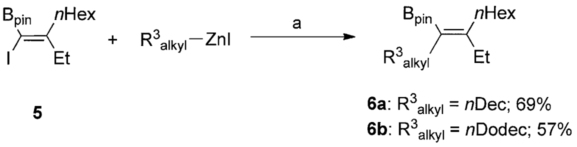
Prior to hydrolysis, the intermediate zirconacyclopentenes **A**[23] formed in situ can serve as versatile precursors of tetrasubstituted olefins bearing a boron functionality. For example, as shown in Scheme 2, the selective protonolysis of a Zr–C(sp^3) bond with isopropyl alcohol, and subsequent one-pot palladium-catalyzed coupling reactions with iodomethane in the presence of CuCl,[24] and iodolysis[23] afforded 1,2,2-trifunctionalized alkenylboronates **4** and **5** in a stereocontrolled manner (68 and 84 % yield, respectively).



Scheme 2. Reagents and conditions: Synthesis of **4**: a) *i*PrOH (0.8 equiv), RT, 1 h; b) then CuCl (1.2 equiv), DMPU (1.8 equiv), [Pd(PPh_3)$_4$] (10 mol %), iodomethane (2.0 equiv), THF, 50 °C, 1 h. Synthesis of **5**: c) *i*PrOH (0.8 equiv), RT, 1 h; d) then I_2 (1.0 equiv), RT, 12 h. DMPU = 1,3-dimethylhexahydro-2-pyrimidinone, THF = tetrahydrofuran.

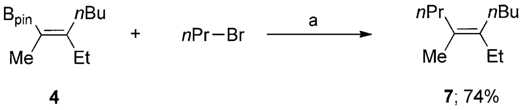
An additional motivation for this study is our interest in developing an efficient route to various tetraalkylated olefins bearing longer alkyl chains that are not readily available. However, the introduction of longer carbon chains containing β-hydrogen atoms proved challenging. For example, our attempt to perform one-pot cross-coupling of the intermediate alkenylzirconocene complex with 1-bromodecane under Fu's conditions (2.5 % of Pd(OAc)$_2$, 2.0 equiv of LiBr, NMP/THF (1:1), 55 °C, 24 h)[25] afforded no product. Presumably, the steric bulk of the tetrasubstituted alkenyl(alkoxy)zirconocene complex suppresses the desired reaction. We thus developed an alternate strategy to introduce the longer alkyl chains bearing β-hydrogen atoms that involved a Negishi coupling of the isolated 1-iodoalkenylboronate **5** and alkylzinc reagents.[26]

We investigated the Negishi coupling reactions of **5** with alkylzinc iodides under several reaction conditions. PEPPSI,[27] recently introduced by Organ and co-workers, displayed the necessary catalytic activity in THF and afforded 1,2,2-trialkylated alkenylboronate **6a** in 42 % yield (based on GC analysis), albeit along with a considerable amount (>15 %) of the undesired protodeiodinated product **2a**. We found that [PdCl$_2$(dppf)][28] was the best catalyst and afforded **6a** in 60 % yield (based on GC analysis).[29] Solvent and additive effects greatly influenced the yield of the reaction; DMI as a solvent with NEt$_3$ as an additive (7:1) furnished **6a** in 75 % yield (based on GC analysis, 69 % yield of isolated product; Scheme 3).[30] The *n*-dodecyl analogue **6b** was synthesized under identical conditions and was isolated in 57 % yield (Scheme 3). Notably, the reaction is highly stereoselective (> 99:1 as determined by ^{1}H NMR spectroscopy) because isomerization during Negishi cross-coupling was suppressed and resulted in retention of configuration. During the reactions, the boron moieties remained intact.[31]



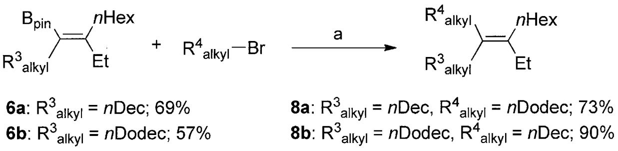
Scheme 3. Reagents and conditions: a) **5** (1 mmol), alkylzinc reagents (1.5 mmol), [PdCl$_2$(dppf)] (4.5 mol %), DMI/NEt$_3$ (7:1), 60 °C, 12 h. DMI = 1,3-dimethyl-2-imidazolidinone, dppf = 1,1′-bis(diphenylphosphanyl)ferrocene.

Our route to the tetraalkylated olefin **7** bearing four different substituents involved the aforementioned Suzuki–Miyaura cross-coupling reaction of **4** and 1-bromopropane (Scheme 4). Compound **7** is the first example of a regio- and stereocontrolled tetrasubstituted olefin that contains four different linear unfunctionalized alkyl groups.[32]



Scheme 4. Reagents and conditions: a) **4** (1 mmol), 1-bromopropane (1.3 mmol), KOH (3 mmol), [Pd(dba)$_2$] (5 mol %), [HP*t*Bu$_2$Me]BF$_4$ (15 mol %), THF, 20 °C, 24 h.

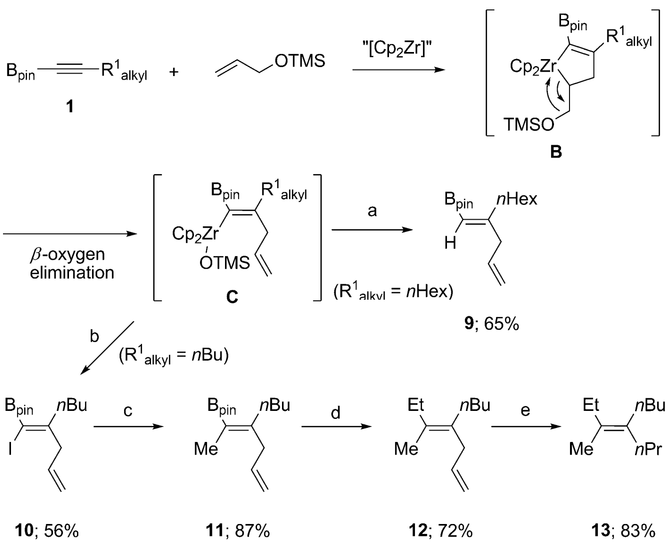
In the same manner the 1,2,2-trialkylated alkenylboronates **6a** and **6b** were subjected to Suzuki–Miyaura coupling with 1-bromoalkanes and afforded tetraalkylated olefins **8a** and **8b** as the pure stereoisomer in 73 % and 90 % yields, respectively, (Scheme 5).[33] The two reactions, thus, complement each other and provide access to various tetrasubstituted olefins, in which all alkyl groups contain β-hydrogen atoms.



Scheme 5. Reagents and conditions: a) **6** (0.5 mmol), 1-bromoalkanes (0.78 mmol), KOH (1.8 mmol), [Pd(dba)$_2$] (5 mol %), [HP*t*Bu$_2$Me]BF$_4$ (15 mol %), THF, 20 °C, 24 h.

To achieve the introduction of hydrocarbon functionalities other than ethyl, we chose a zircono/allylation approach,[34] as summarized in Scheme 6. Srebnik and co-workers have reported that the phosphine-stabilized borylzirconacyclopropene species were formed by the reactions of 1-alkynylboronates **1** with the Negishi reagent in the presence of tributylphosphine.[35] The added allyloxytrimethylsilane rapidly reacted with the intermediate zirconacyclopropenes to form the zirconacyclopentene **B** in a regioselective manner with the boron moiety at the α position. The spontaneous β-oxygen elimination resulted in the formation of a transient alkenylzirconocene intermediate **C**. Hydrolysis of the remain-

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 6. Regio- and stereoselective synthesis of the tri- and tetrasubstituted alkenylboronates **9–11** and the cross-coupled tetra-substituted olefins **12** and **13**. Reagents and conditions: a) [Cp$_2$ZrCl$_2$] (1.2 equiv), *n*BuLi (2.4 equiv), tributylphosphine (1.2 equiv), −78 °C to RT, 1 h; then **1a** (1.0 equiv), allyloxytrimethylsilane (1.5 equiv), 50 °C, 1 h; then hydrolysis; b) [Cp$_2$ZrCl$_2$] (1.2 equiv), Mg (3.0 equiv), **1c** (1.2 equiv), allyloxytrimethylsilane (1.0 equiv), 50 °C, 1 h; then I$_2$ (2.0 equiv), RT, 12 h; c) ZnBr$_2$ (1.65 equiv), MeMgBr (1.35 equiv), THF, 0 °C, 30 min; then **10** (1.0 equiv), [Pd(PPh$_3$)$_4$] (2 mol %), RT, 18 h; d) **11** (1.0 equiv), bromoethane (1.3 mmol), KOH (3 mmol), [Pd(dba)$_2$] (5 mol %), [HP*t*Bu$_2$Me]BF$_4$ (15 mol %), THF, 20 °C, 12 h; e) [RhCl(PPh$_3$)$_3$] (10 mol %), H$_2$, benzene, RT, 18 h. TMS = trimethylsilyl.

ing Zr−C bond delivered the trisubstituted alkenylboronate **9** in 65 % yield. Again, the regioselectivity of **9** was determined by ^{1}H NMR spectroscopy. As can be seen in the ^{1}H NMR spectra the presence of a triplet in the double bond region (around 5.14 ppm) is indicative of the vinyl hydrogen atom that is located at the α position with respect to the boryl groups.

1-Iodo-1-alkenylboronate **10** was then synthesized from **1** using allyloxytrimethylsilane by initial zirconacycle formation with [Cp$_2$ZrCl$_2$]/Mg,[36] and subsequent iodonolysis in 56 % yield. The palladium-catalyzed alkylation[37] with MeZnBr in the presence of 2 mol % of [Pd(PPh$_3$)$_4$] in THF afforded the methylated alkenylboronate **11** in 87 % yield with >99 % isomeric purity.[38] Compound **11** was subjected to the palladium-catalyzed Suzuki–Miyaura coupling with bromoethane and afforded **12** in 72 % yield.[39] Finally a chemoselective catalytic hydrogenation of **12** with 10 mol % of Wilkinson's catalyst was performed to deliver **13**, a structural isomer of **7**, in >99 % isomeric purity and 83 % yield.

In summary, we have developed a versatile, direct synthesis of multialkylated olefins bearing various alkyl groups by a regioselective formation of zirconacyclopentene species using alkynylboronates followed by successive palladium-catalyzed Negishi and Suzuki–Miyaura cross-coupling reactions. This method is practical and simple, and more importantly, provides the products as single isomers (selectivity >99 %). Furthermore, the addition of β-hydrogen-containing alkyl electrophiles to alkenylboronates and the reaction of 1-iodo-1-borylethenes with alkylzinc reagents expands the cross-coupling repertoire. Further studies to develop a cross-coupling with secondary alkyl functionalities and the application of this approach to the synthesis of natural products will be the subject of forthcoming papers.

Received: May 26, 2011
Published online: August 9, 2011

Keywords: cross-coupling · Negishi coupling · palladium · Suzuki–Miyaura coupling · zirconacycles

---

[1] a) A. B. Flynn, W. W. Ogilvie, *Chem. Rev.* **2007**, *107*, 4698–4745; b) E. Negishi, Z. Huang, G. Wang, S. Mohan, C. Wang, H. Hattori, *Acc. Chem. Res.* **2008**, *41*, 1474–1485.

[2] For example, carbomagnesation/Kumada–Tamao–Corriu coupling, see: a) K. Murakami, H. Ohmiya, H. Yorimitsu, K. Oshima, *Org. Lett.* **2007**, *9*, 1569–1571; carbozincation/Negishi coupling: b) K. Murakami, H. Yorimitsu, K. Oshima, *Org. Lett.* **2009**, *11*, 2373–2375; stannyllithiation/Migita–Kosugi–Stille coupling: c) E. Nakamura, H. Tsuji, Y. Ueda, L. Ilies, *J. Am. Chem. Soc.* **2010**, *132*, 11 854–11 855.

[3] a) K. Itami, T. Kamei, J.-i. Yoshida, *J. Am. Chem. Soc.* **2003**, *125*, 14670–14671; b) C. Zhou, R. C. Larock, *J. Org. Chem.* **2005**, *70*, 3765–3777; c) M. Shimizu, C. Nakamaki, K. Shimono, M. Schelper, T. Kurahashi, T. Hiyama, *J. Am. Chem. Soc.* **2005**, *127*, 12506–12507; d) Z. Tan, E. Negishi, *Angew. Chem.* **2006**, *118*, 776–779; *Angew. Chem. Int. Ed.* **2006**, *45*, 762–765; e) J. Simard-Mercier, A. B. Flynn, W. W. Ogilvie, *Tetrahedron* **2008**, *64*, 5472–5481; f) N. Ishida, Y. Shimamoto, M. Murakami, *Org. Lett.* **2009**, *11*, 5434–5437; g) K. Endo, M. Hirokami, T. Shibata, *J. Org. Chem.* **2010**, *75*, 3469–3472.

[4] For representative syntheses of tri- and tetraalkylated olefins, see: a) T. P. Holler, A. Spaltenstein, E. Turner, R. E. Klevit, B. M. Shapiro, P. B. Hopkins, *J. Org. Chem.* **1987**, *52*, 4421–4423; b) L. Anastasia, Y. R. Dumond, E. Negishi, *Eur. J. Org. Chem.* **2001**, 3039–3043; c) J. Gerard, L. Hevesi, *Tetrahedron* **2004**, *60*, 367–381.

[5] a) V. Fiandanese, *Pure Appl. Chem.* **1990**, *62*, 1987–1992; b) T. Itoh, K. Sakabe, K. Kudo, P. Zagatti, M. Renou, *Tetrahedron Lett.* **1998**, *39*, 4071–4074; c) B. Kang, R. Britton, *Org. Lett.* **2007**, *9*, 5083–5086.

[6] a) T. Nakata, G. Schmid, B. Vranesic, M. Okigawa, T. Smith-Palmer, Y. Kishi, *J. Am. Chem. Soc.* **1978**, *100*, 2933–2935; b) A. Migita, Y. Shichijo, H. Oguri, M. Watanabe, T. Tokiwano, H. Oikawa, *Tetrahedron Lett.* **2008**, *49*, 1021–1025.

[7] E. J. Corey, J. A. Katzenellenbogen, N. W. Gilman, S. A. Roman, B. W. Erickson, *J. Am. Chem. Soc.* **1968**, *90*, 5618–5620.

[8] A. W. Hofmann, *Liebigs Ann. Chem.* **1851**, *78*, 253–286.

[9] A. M. Saytzeff, *Liebigs Ann. Chem.* **1875**, *179*, 296–301.

[10] Y. Nishihara, M. Miyasaka, M. Okamoto, H. Takahashi, E. Inoue, K. Tanemura, K. Takagi, *J. Am. Chem. Soc.* **2007**, *129*, 12634–12635.

[11] Y. Nishihara, D. Saito, K. Tanemura, S. Noyori, K. Takagi, *Org. Lett.* **2009**, *11*, 3546–3549.

[12] For reviews of the Negishi coupling, see: a) E. Negishi, F. Liu in *Metal-Catalyzed Cross-Coupling Reactions,* Chapter 1 (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, New York, **1998**; b) E. Negishi in *Handbook of Organopalladium Chemistry for Organic Synthesis* (Ed.: E. Negishi), Wiley-Interscience, New York, **2002**, pp. 229–247.

[13] For reviews of the Suzuki–Miyaura coupling, see: a) A. Suzuki in *Handbook of Organopalladium Chemistry for Organic Synthesis*

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

(Ed. E. Negishi), Wiley-Interscience, New York, **2002**, pp. 249–262; b) N. Miyaura, *Top. Curr. Chem.* **2002**, *219*, 11–59; c) S. Kotha, K. Lahiri, D. Kashinath, *Tetrahedron* **2002**, *58*, 9633–9695; d) A. Suzuki in *Metal-Catalyzed Cross-Coupling Reactions*, Chapter 2 (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, New York, **1998**; e) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457–2483.

[14] For papers outlining the synthetic utility of 1-alkynylboronates, see: a) Y. Nishihara, M. Okamoto, Y. Inoue, M. Miyazaki, M. Miyasaka, K. Takagi, *Tetrahedron Lett.* **2005**, *46*, 8661–8664; b) M. Suginome, M. Shirakura, A. Yamamoto, *J. Am. Chem. Soc.* **2006**, *128*, 14438–14439; c) D. L. Browne, J. F. Vivat, A. Plant, E. Gomez-Bengoa, J. P. A. Harrity, *J. Am. Chem. Soc.* **2009**, *131*, 7762–7769.

[15] a) E. Negishi, F. E. Cederbaum, T. Takahashi, *Tetrahedron Lett.* **1986**, *27*, 2829–2832; b) E. Negishi, T. Takahashi, *Acc. Chem. Res.* **1994**, *27*, 124–130.

[16] a) T. Takahashi, Z. Xi, C. J. Rousset, N. Suzuki, *Chem. Lett.* **1993**, *22*, 1001–1004; b) Z. Xi, R. Hara, T. Takahashi, *J. Org. Chem.* **1995**, *60*, 4444–4448.

[17] When the zirconacyclopentene was formed from [Cp_2ZrCl_2]/2 EtMgBr in the absence of an ethylene atmosphere, the yields of the desired alkenylboronates **2** were lower. For example, for **2a**, 81% vs. 56% yield.

[18] A. Quntar, M. Srebnik, *Org. Lett.* **2004**, *6*, 4243–4244.

[19] a) T. Takahashi, Y. Nitto, T. Seki, M. Saburi, E. Negishi, *Chem. Lett.* **1990**, *19*, 2259–2262; b) T. Takahashi, T. Seki, Y. Nitto, M. Saburi, C. J. Rousset, E. Negishi, *J. Am. Chem. Soc.* **1991**, *113*, 6266–6268.

[20] Y. Nishihara, Y. Inoue, M. Fujisawa, K. Takagi, *Synlett* **2005**, 2309–2312.

[21] K. Tonogaki, K. Soga, K. Itami, J.-i. Yoshida, *Synlett* **2005**, 1802–1804.

[22] J. H. Kirchhoff, M. R. Netherton, I. D. Hills, G. C. Fu, *J. Am. Chem. Soc.* **2002**, *124*, 13662–13663.

[23] S. Ben-Valid, A. A. Quntar, M. Srebnik, *J. Org. Chem.* **2005**, *70*, 3554–3559.

[24] a) T. Takahashi, R. Hara, Y. Nishihara, M. Kotora, *J. Am. Chem. Soc.* **1996**, *118*, 5154–5155; b) R. Hara, Y. Nishihara, P. D. Landre, T. Takahashi, *Tetrahedron Lett.* **1997**, *38*, 447–450.

[25] S. L. Wiskur, A. Korte, G. C. Fu, *J. Am. Chem. Soc.* **2004**, *126*, 82–83.

[26] R. Jana, T. P. Pathak, M. S. Sigman, *Chem. Rev.* **2011**, *111*, 1417–1492.

[27] a) C. J. O'Brien, E. A. B. Kantchev, C. Valente, N. Hadei, G. A. Chass, A. Lough, A. C. Hopkinson, M. G. Organ, *Chem. Eur. J.* **2006**, *12*, 4743–4748; b) M. G. Organ, S. Avola, I. Dubovyk, N. Hadei, E. A. B. Kantchev, C. J. O'Brien, C. Valente, *Chem. Eur. J.* **2006**, *12*, 4749–4755.

[28] T. Hayashi, M. Konishi, Y. Kobori, M. Kumada, T. Higuchi, K. Hirotsu, *J. Am. Chem. Soc.* **1984**, *106*, 158–163.

[29] Notes: $Pd(OAc)_2$ (5 mol%) was used as a catalyst with various phosphine ligands; dppe (17%), dppp (52%), Ruphos (53%), Xphos (53%), and Xantphos (38%).

[30] Notes: NEt_3 alone (42%), THF/NEt_3 (7:1; 61%), and DMF/NEt_3 (7:1; 65%).

[31] It has been reported that 1,1-borylzinc reagents can be with 1-iodo-1-octene under Negishi conditions, in which the boron functionalities are compatible, see: J. R. Waas, A. R. Sidduri, P. Knochel, *Tetrahedron Lett.* **1992**, *33*, 3717–3720.

[32] This compound has been proposed as a propylene tetramer, but no spectroscopic data was available: CAS-number [303962–00–7]. See: Y. T. Vigranenko, *Kinet. Catal.* **2000**, *41*, 451–456.

[33] Most signals assigned to the alkyl carbon atoms of **8a** appeared at almost the same chemical shifts as those of **8b** in their $^{13}C\{^{1}H\}$ NMR spectra. However, their expanded spectra in a range of 29–30 ppm indicates that there is a slight difference between the alkyl signals. See the Supporting information.

[34] T. Takahashi, N. Suzuki, M. Kageyama, D. Y. Kondakov, R. Hara, *Tetrahedron Lett.* **1993**, *34*, 4811–4814.

[35] a) A. A. Quntar, A. Botvinik, A. Rubinstein, M. Srebnik, *Chem. Commun.* **2008**, 5589–5591; b) A. Botvinik, A. A. Quntar, A. Rubinstein, M. Srebnik, *J. Organomet. Chem.* **2009**, *694*, 3349–3352.

[36] N. Suzuki, D. Hashizume, H. Yoshida, M. Tezuka, K. Ida, S. Nagashima, T. Chihara, *J. Am. Chem. Soc.* **2009**, *131*, 2050–2051.

[37] E. Negishi, Y. Zhang, F. E. Cederbaum, M. B. Webb, *J. Org. Chem.* **1986**, *51*, 4080–4082.

[38] A one-pot palladium-catalyzed methylation from **C** through transmetalation to copper gave a lower yield of product.

[39] The configuration of **12** was unambiguously confirmed by an NOESY measurement. See the Supporting Information.

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim