Zinc Borates: Functionalized Hard Nucleophiles for Coupling Reactions with Secondary Allylic Acetates

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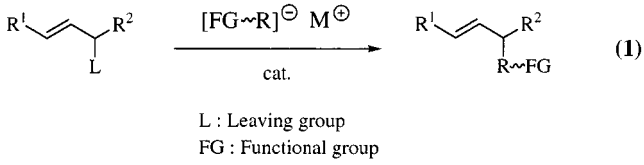
Keywords: Allyl acetates / Borates / C−C coupling / Nickel / Zinc

We have succeeded in developing zinc borates of the general structure **3** for coupling reaction with allylic acetates. The advantages of using compounds **3** are their compatibility with carbonyl groups such as aldehyde, ketone, and ester groups, and their high reactivity toward secondary allylic acetates. Zinc borates **3** were prepared from boronate esters **1** [R^T = *p*-(CHO)C_6H_4, *p*-(Ac)C_6H_4, *p*-{Ac$(CH_2)_2$}C_6H_4, *p*-(AcOCH_2)C_6H_4, *p*-{AcO$(CH_2)_3$}C_6H_4, *p*-{$EtO_2C(CH_2)_2$}C_6H_4, (*E*)-CH=CH$(CH_2)_4$OAc] with MeZnCl; subsequent treatment with allylic acetates **4** [R = *n*-C_5H_{11}, *c*-C_6H_{11}, $(CH_2)_2$CH(−O$(CH_2)_2$O−)] in the presence of $NiCl_2(PPh_3)_2$ (10 mol-%) in THF–DMI (1,3-dimethyl-2-imidazolidinone) (10 equiv.) at 40–50 °C overnight furnished the coupling products **5** in good yields. Among the products, **5bb**, possessing one free and one protected aldehyde group, is a highlight of this type of reaction. The stereochemical aspects of the reaction were also examined. Thus, the alkenyl groups of (*E*)- and (*Z*)-alkenyl borates **3b** and **c** were transformed with retention of the olefinic geometry into acetates **4a** and **b** (R = *n*-C_5H_{11}, *c*-C_6H_{11}), while reaction of cyclic acetate **11** proceeded with inversion at the carbon center involved in the reaction. In addition, we found that the anions generated from $(EtO)_2P(=O)CH_2CO_2Et$ and $(MeO)_2P(=O)CH_2Ac$ under Masamune's conditions attacked the aldehyde carbon in the boronate **1d** to produce — after reduction of the double bond — the boronate esters **1i** and **1j**, respectively, in good yields.

Introduction

Transition metal-catalyzed coupling is a most reliable method in organic synthesis for formation of carbon−carbon bonds.[1] The reaction proceeds with retention of stereochemistry at the reaction sites, which are usually inactive to classical reagents such as organolithiums and -magnesiums. Much effort has been made to develop the synthetic advantages of the reaction, with regard to reactivity, entry of substrates, and catalysts. Also important is compatibility with functional groups reactive toward nucleophiles. Organoborons,[2] -tins,[3] and -zincs[4] are such reagents that are compatible with reactive functional groups. With boron and tin reagents, several methods that tolerate carbonyl and/or hydroxyl groups have been developed, and the coupling reaction with aryl and alkenyl substrates proceeds efficiently.[2,3] However, these reagents suffer from low reactivity toward allylic substrates [Equation (1)] because of the stable nature of the carbon−metal bond in the transient π-allyl intermediates.[5,6,7]



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On the other hand, classical zinc reagents of the general formula, RZnX, show high reactivity toward allylic substrates as well as towards aryl and alkenyl substrates.[8] They are prepared, however, from ZnX_2 and lithium or magnesium reagents. Consequently, it is difficult to apply this preparation to functionalization of zinc reagents.[4] In order to overcome the limitations of these reagents, much attention has recently been focused on preparation and reaction of functionalized organozincs. Homoenolates,[9] low temperature lithiation of halides followed by reaction with ZnX_2,[10] insertion of zinc into halo compounds,[11] hydrozincation of alkenes,[12,13b] zinc exchanges,[13,14] and electrochemical methods[15] are among those explored recently. These modern organozincs show almost the same reactivity as those prepared from ZnX_2 and classical reagents.[16] However, allylic coupling is awkward. An attempt by Tamaru resulted in homocoupling.[17] Therefore, transmetallation to more reactive copper reagents is necessary if successful allylic coupling is to be achieved.[11h,13a,16,18,19] Even then, allylic substrates are limited to halides. In other words, the most important advantage of the allylic coupling reaction, the creation of a chiral carbon-carbon bond from secondary allylic substrates, is not fully realized with allylic halides since preparations of these halides are limited to primary ones. Unlike the halides, secondary allylic alcohols are available quite easily. Consequently, we began investigations to find a new reagent/catalyst system for a coupling reaction — in which the reagents were compatible with several kinds of carbonyl groups — with derivatives of secondary allylic alcohols.

Recently, we found that the lithium borates **2**, prepared from the boronate esters **1** and MeLi [Equation (2)], possess high reactivity towards secondary allylic alcohol derivatives in the presence of a nickel catalyst and that the neutral nature of **2** allows an ester and/or hydroxy group to be present

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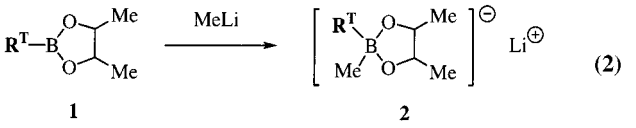

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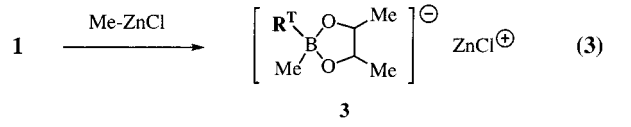
in the allylic substrates.[20] We saw from this result that if we could find an organometallic reagent which attacks the central boron atom faster than a functional group present in the boronate ester, this would provide a pathway to functionalized hard nucleophiles for coupling with secondary allylic alcohol derivatives. We found that MeZnCl was the reagent of choice [Equation (3)], and that coupling reactions between allylic acetates **4** and zinc borates **3** generated with MeZnCl proceeded efficiently (in the presence of $NiCl_2(PPh_3)_2$ (10 mol-%) in THF−DMI (1,3-dimethyl-2-imidazolidinone) overnight at 40−50 °C) to afford coupling products **5** [Equation (4)]. Here we report the results of our investigation of this coupling reaction in full.[21]



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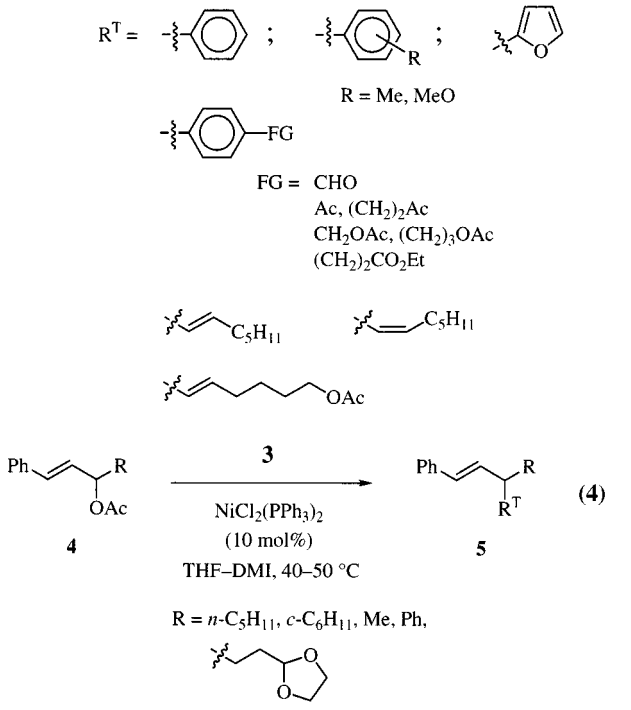


Results and Discussion

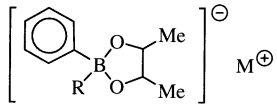
Finding Zinc Borates

For the preliminary study, the phenylboronate ester **1a** (R^T = Ph) and allylic acetate **4a** (R = *n*-C_5H_{11}) were chosen as a representative precursor of the borate and as the substrate. Several organometallics with low nucleophilicities towards carbonyl groups were examined with regard to the preparation of the corresponding borates. Conversion of **1a** (2.7−3.5 equiv. relative to **4a**) into the borate was studied with the aid of an organometallic reagent (2.5−3.3 equiv.) in THF between 0 °C and room temperature for 0.5−4 h, and the borates **3a** (R^T = Ph) (= **6** with R = Me, M = ZnCl) or **6a**−**g**, which were presumed to be produced from other organometallics, were subjected to coupling reaction conditions with acetate **4a** in the presence of 10 mol-% of $NiCl_2(PPh_3)_2$ overnight, at or above room temperature (Table 1).

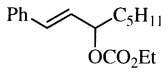
Table 1. Preliminary results of the coupling reaction with acetate **4a** (R = *n*-C_5H_{11})

Entry	Borate	R	M	Result
1	**6a**	Me	Cu	NR[a]
2	**6b**	Me	Ti(O-*i*Pr)$_3$	NR[a]
3	**3a** (= **6** of R = Me, M = ZnCl)			**5a**[b] (88%)[c]
4	**6c**	Me	ZnBr	**5a**[d] (85%)[c]
5	**6d**	Me	ZnI	**5a**[e] (77%)[c]
6	**6e**	Me	ZnF	NR[a]
7	**6f**	*n*Bu	ZnCl	Complex mixture[f]
8	**6g**	Et	ZnEt	Complex mixture[g]

[a] No reaction. − [b] **5a** (R^T = Ph, R = *n*-C_5H_{11}): **9**:**10** = 91:5:4. The result is also given in entry 1 of Table 2. − [c] Isolated yield. − [d] **5a**:**9**:**10** = 94:4:2. − [e] **5a**:**9**:**10** = 90:5:5. − [f] **5a**:**8a**:**8b** = 4:34:62. − [g] **5a**:**8a**:**8b** = 10:45:45.



6 : M = Cu, Ti(O-*i*-Pr)$_3$, ZnX
R = Me, Et, *n*-Bu



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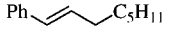
We initially examined the reaction using the supposed copper or titanium borates **6a** and **6b** at 40−60 °C overnight, which resulted in recovery of acetate **4a** and boronate ester **1a** (entries 1 and 2). The boronate ester, in contrast to organoboranes with an alkyl group as a dummy ligand,[22] was less reactive toward MeCu. The desired reaction was achieved with zinc borate **3a** at 40−50 °C, furnishing **5a** (R^T = Ph, R = *n*-C_5H_{11}) as the major product (entry 3). The reaction temperature of 40−50 °C was necessary for reproducibility; at room temperature it was capricious. Zinc borates **6c** and **6d** provided similar results (entries 4,5). Other zinc borates **6e**−**g** were less effective, resulting either in no reaction (entry 6), or in the production of a complex mixture in which olefins **8a** and **8b** were detected by TLC and ^1H NMR spectroscopy (entries 7, 8).



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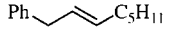

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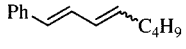

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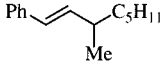

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Other parameters of the reaction were investigated with borate **3a** under the conditions described above [10 mol-% of $NiCl_2(PPh_3)_2$, THF, 40−50 °C, overnight: entry 1 of Table 2]. For the substrate, the same reactivity was observed with carbonate **7** (entries 1 and 7). A nickel complex $NiCl_2$(dppf) showed similar potency as a catalyst (entries 1 vs. 2, and 7 vs. 8). A reaction time of 30 min at room temperature was sufficient for preparation of borate **3a**, and the coupling was completed within 12 h. In all cases, neither the regioisomer nor the *cis* isomer was detected by ^{1}H NMR spectroscopy (300 MHz). Palladium complexes such as $PdCl_2(PPh_3)_2$ and $Pd(PPh_3)_4$ were ineffective for this coupling. Since diene **9** and methyl-coupling product **10** were, in most cases, produced as by-products (2−8% each), investigation was continued further. It was found that their production could be suppressed to less than 2% combined yield by addition of DMI or DMF (10 equiv.) (entries 5 and 6), although such by-products, if present at all, were easily separated by silica gel chromatography.

Table 2. Preliminary results of the coupling reaction of **4a** or **7** with zinc borate **3a** (R^T = Ph)

Entry[a]	Substrate	Catalyst[b]	Polar solvent[c]	Yield (%) of **5a**[d]	Ratio **5a**:**9**:**10**[e]
1	**4a**	$NiCl_2(PPh_3)_2$	−	88	91:5:4
2	**4a**	$NiCl_2$(dppf)	−	81	91:3:6
3	**4a**	$NiCl_2(PPh_3)_2$	MeCN	78	89:6:5
4	**4a**	$NiCl_2(PPh_3)_2$	DMSO	83	89:6:5
5	**4a**	$NiCl_2(PPh_3)_2$	DMI	87	>98:<1:<1
6	**4a**	$NiCl_2(PPh_3)_2$	DMF	80	>98:<1:<1
7	**7**	$NiCl_2(PPh_3)_2$	−	88	92:4:4
8	**7**	$NiCl_2$(dppf)	−	84	90:2:8

[a] Carried out at 40−50 °C overnight. − [b] 10 mol-%. − [c] Added 10 equiv. in a THF solution. − [d] Isolated yield by chromatography. − [e] Determined by ^{1}H NMR (300 MHz) spectroscopy.

Regarding the production of **10**, reaction of acetate **4a** and MeZnCl (3 equiv.) was examined under the conditions indicated in Equation (4). The reaction proceeded slowly to afford **9** and **10** in 42% and 28% yields, respectively. On the other hand, reaction of **1a** with MeZnCl at room temperature for 30 min was sufficient for generation of borate **3a**, as was confirmed by complete disappearance of **1a** on TLC. These results show that **3a**, formed from MeZnCl and **1a**, is really the species that produces **10** as the by-product, but to a lesser extent. We are now studying the precise role played by DMI in the substantial suppression of methyl transfer.

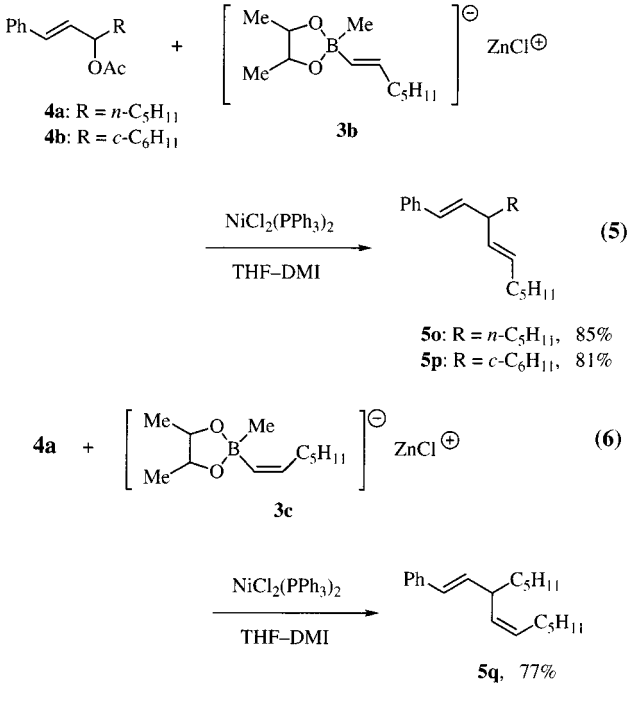
Generality of the New Coupling System

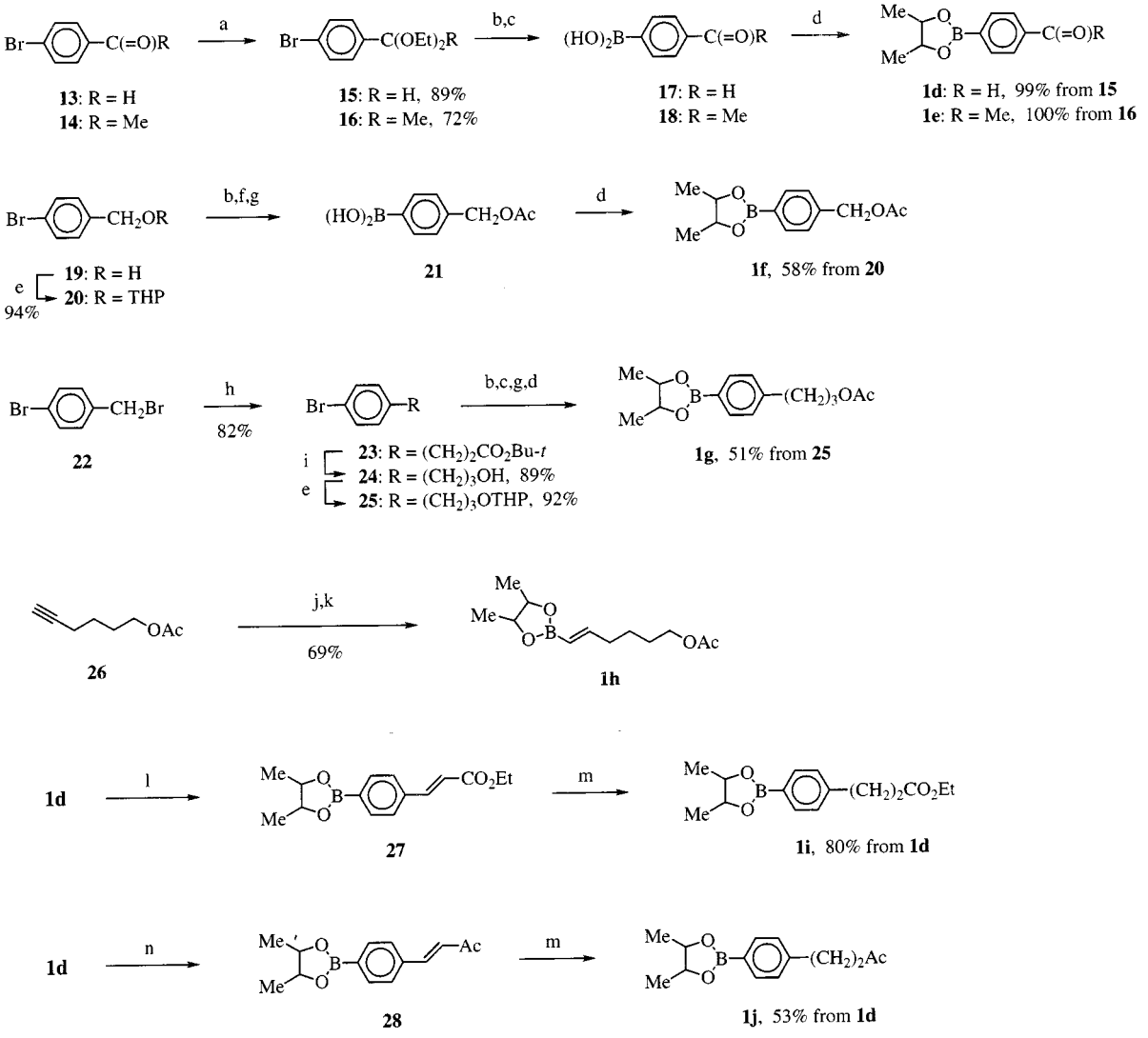
The optimized conditions described above (Table 2, entry 5) were applied to reactions between zinc borates **3**, with phenyl, methylphenyl, or methoxyphenyl substituents as R^T groups, and acetates **4a** (R = *n*-C_5H_{11}), **4b** (R = *c*-C_6H_{11}), **4c** (R = Me), and **4d** (R = Ph) (Equation 4). The results are summarized in Table 3. Reaction of the Me- or MeO-substituted aryl boronate esters **1** (2.7−3.5 equiv.) with MeZnCl (2.5−3.3 equiv.), and subsequent coupling with **4a** in the presence of $NiCl_2(PPh_3)_2$ (5−10 mol-%) and DMI (10 equiv.), furnished **5b**−**f** in good yields, regardless of the substituent pattern on the aromatic ring (entries 1−5).[23] The furyl boronate ester **1** (R^T = 2-furyl) also furnished the product **5g** in good yield (entry 6). The excellent reactivity of **3** did not place any restriction on allylic acetates. Thus, other acetates **4** with a substituent R of different size (*c*-C_6H_{11}, Me, Ph) efficiently afforded **5h**−**n** (entries 7−13).[23] Noteworthy is the fact that the sterically hindered boronate esters **1** (R^T = *o*-MeC_6H_4, *o*-$MeOC_6H_4$) are converted into the corresponding borates and that, more importantly, these borates keep their high reactivity toward acetate **4a** and the more bulky acetate **4b** (entries 1,4,8).

Table 3. Nickel-catalyzed coupling reaction of acetate **4a**−**d** and zinc borates **3** in the presence of DMI

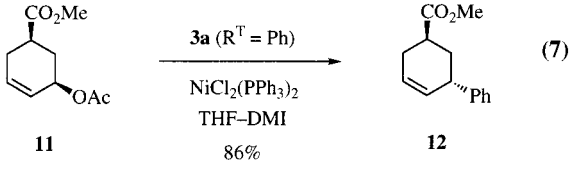
Entry[a]		R	R^T	Yield %[b]
1	**5b**	*n*-C_5H_{11}	*o*-MeC_6H_4	89
2	**5c**	*n*-C_5H_{11}	*m*-MeC_6H_4	81
3	**5d**	*n*-C_5H_{11}	*p*-MeC_6H_4	87
4[c]	**5e**	*n*-C_5H_{11}	*o*-$MeOC_6H_4$	88
5	**5f**	*n*-C_5H_{11}	*p*-$MeOC_6H_4$	76
6	**5g**	*n*-C_5H_{11}	2-furyl	95
7	**5h**	*c*-C_6H_{11}	Ph	94
8	**5i**	*c*-C_6H_{11}	*o*-MeC_6H_4	82
9	**5j**	*c*-C_6H_{11}	*p*-MeC_6H_4	87
10	**5k**	*c*-C_6H_{11}	*p*-MeC_6H_4	98
11	**5l**	Me	Ph	83
12	**5m**	Ph	Ph	95
13	**5n**	Ph	*p*-$MeOC_6H_4$	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] Combined yields of the by-products (the diene and the Me−coupling product) were <2% by ^{1}H NMR spectroscopy. − [c] Carried out without DMI.





Scheme 1. (a) $HC(OEt)_3$, H^+, EtOH; (b) *n*BuLi, −78 °C, then $B(O\text{-}iPr)_3$, THF; (c) H_3O^+; (d) 2,3-butanediol, $MgSO_4$; (e) DHP, *p*-TsOH·H_2O (cat.); (f) *p*-TsOH·H_2O (cat.), EtOH; (g) Ac_2O, C_5H_5N; (h) $MeCO_2tBu$, LDA, THF−DMSO; (i) DIBAL, toluene; (j) $(Ipc)_2BH$ then MeCHO; (k) 2,3-butanediol, THF; (l) $(EtO)_2P(=O)CH_2CO_2Et$, LiCl, DBU; (m) H_2, Pd/C; (n) $(MeO)_2P(=O)CH_2Ac$, LiCl, iPr_2NEt



(7)

Stereochemical aspects of the reaction were next studied, using borates possessing a *trans* or *cis* alkenyl group as an R^T group, or cyclohexenyl acetate **11**.[24] Reaction of acetate **4a** with alkenyl borates **3b** and **3c**, prepared from the corresponding boronate esters and MeZnCl, proceeded with retention of the alkenyl stereochemistry to produce **5o** and **5q**, respectively, in good yields [Equation (5) and Equation (6)]. The ^1H NMR spectra of **5o** and **5q** clearly indicate that neither product was contaminated with the other isomer. Retention of the olefinic geometry of **3b** was also confirmed in the reaction with acetate **4b**, giving **5p** in 81% yield [Equation (5)]. Inversion of stereochemistry at the carbon possessing the AcO group was observed in the reaction between acetate **11** and borate **3a**, furnishing **12** in 86% yield [Equation (7)]. This result indicates that the reaction proceeds through the widely accepted mechanism involving oxidative addition with inversion of configuration, transmetallation, and reductive elimination with retention of configuration.[6]

Preparation and Reaction of Functionalized Boronate Esters

For this study, boronate esters **1d**−**j**, possessing an aldehyde, ketone, or ester group, were prepared by the reaction sequences shown in Scheme 1. To avoid side reactions at the electrophilic boron atom in the boronate esters, the moiety containing the boron atom was installed at a later stage in the preparation of boronate esters **1d** and **1e**. Thus, acetals **15** and **16**, derived from **13** and **14**, respectively, were converted into the lithium anions, which yielded boronic acids **17** and **18** upon reaction with $B(O\text{-}iPr)_3$ and subsequent hydrolysis, according to the literature procedure.[25] Next, esterification of **17** and **18** with 2,3-butanediol in the pres-

ence of $MgSO_4$ afforded boronate esters **1d** and **e**, respectively, in almost quantitative yields. The same strategy was applied to **20**, furnishing **1f** in 58% yield from **20** through **21**. The preparation of **1g** started from bromide **22**, which was converted into **23** by reaction with the enolate anion derived from $MeCO_2tBu$ and LDA.[26] Reduction of **23** with DIBAL, followed by protection with DHP, afforded **25** in 67% yield from **22**. Installation of the boron component to **25** was achieved as described above, producing **1g** in good yield. Transformation of acetylene **26** into boronate ester **1h** was carried out by the method of Suzuki and Miyaura, using $(Ipc)_2BH$, in 69% yield.[27] Other methods, using catecholborane,[28] pinacolborane,[29] or 2,3-butanediolborane,[30] were less effective for this purpose.

Since the boron-containing aldehyde **1d** had been obtained in large quantity, we explored another possible means of installing an ester or ketone group into it. After several trials, the Wittig−Horner reaction with $(EtO)_2P(=O)CH_2CO_2Et$ and $(MeO)_2P(=O)CH_2Ac$ under the conditions reported by Masamune[31] was found to furnish **27** and **28**, both in good yields; subsequent hydrogenation on Pd/C afforded **1i** and **1j** in 80% and 53% yields, respectively. It is interesting to note that the aldehyde carbon, rather than the boron, is involved in the Wittig reaction. This unusual chemoselectivity may be explained by assuming that reaction of **1d** at the aldehyde carbon and of boron with the phosphonate anion take place *reversibly*, consequently producing the Wittig product, while MeZnCl attacks the boron *irreversibly*, furnishing zinc borate **3d** [R^T = *p*-$(CHO)C_6H_4$] (vide infra).

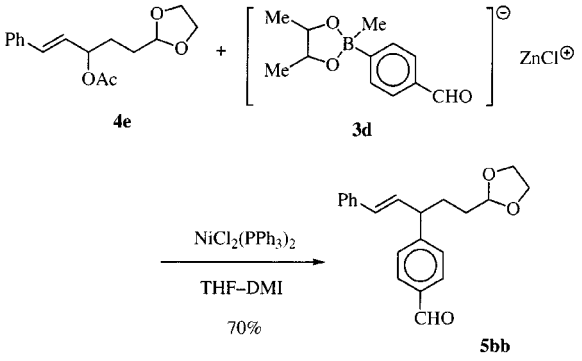
With the above functionalized boronate esters in hand, coupling reactions with allylic acetates **4a** and **4b** (R = *n*-C_5H_{11}, *c*-C_6H_{11}) were carried out under the optimized conditions described above (Equation 4), giving the results summarized in Table 4. In all cases, MeZnCl attacked the boron atom on the boronate esters **1d**−**j** chemoselectively, to form the corresponding borates **3**, and subsequent reaction with acetates **4a** and **4b** afforded coupling products **5r**−**aa** in good yields. Among these, the results obtained with borate **3d** [R^T = *p*-$(CHO)C_6H_4$] are especially noteworthy, since the electron-withdrawing nature of the aldehyde group affected the reactivity only minimally, affording **5r** and **s** in good yields (entries 1,2).

Table 4. Products derived from functionalized boronate esters **1d**−**j**

Entry[a]	5	R	R^T	Yield %[b]
1	**5r**[c]	*n*-C_5H_{11}	*p*-$(CHO)C_6H_4$	75
2	**5s**[c]	*c*-C_6H_{11}	*p*-$(CHO)C_6H_4$	89
3	**5t**	*n*-C_5H_{11}	*p*-$(Ac)C_6H_4$	87
4	**5u**	*c*-C_6H_{11}	*p*-$(Ac(CH_2)_2)C_6H_4$	85
5	**5v**	*n*-C_5H_{11}	*p*-$(AcOCH_2)C_6H_4$	89
6	**5w**	*n*-C_5H_{11}	*p*-$(AcO(CH_2)_3)C_6H_4$	83
7	**5x**	*c*-C_6H_{11}	*p*-$(AcO(CH_2)_3)C_6H_4$	92
8	**5y**	*n*-C_5H_{11}	*p*-$(EtO_2C(CH_2)_2)C_6H_4$	95
9	**5z**	*c*-C_6H_{11}	*p*-$(EtO_2C(CH_2)_2)C_6H_4$	84
10	**5aa**	*n*-C_5H_{11}	(*E*)-$CH=CH(CH_2)_4OAc$	87

[a] Reactions were carried out under the conditions of Equation 4 unless otherwise noted. − [b] Isolated yields. − [c] At 50−60 °C.

The efficiency of this methodology is demonstrated in Equation (8). As can be seen, coupling of **4e** and **3d** afforded **5bb**, which possesses two different aldehyde groups, in 70% yield.



(8)

Conclusion

We have reported zinc borates **3**: the first examples of functionalized hard nucleophiles designed for coupling reactions with allylic alcohol derivatives. These reagents were prepared in 30 min at room temperature from the boronate esters **1** and MeZnCl, and the compatibility of the technique with aldehyde, ketone, and ester groups on aryl and alkenyl reagents has been demonstrated, using the boronate esters **1d**−**1j**. The zinc borates **3** thus prepared showed high reactivity toward secondary allylic acetates **4a**−**e** in the presence of $NiCl_2(PPh_3)_2$ (10 mol-%) in THF−DMI at 40−50 °C, producing **5** in good yields.

Experimental Section

General: Unless otherwise noted, ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were measured in $CDCl_3$ using as internal standards $SiMe_4$ (δ = 0) and the center line of the $CDCl_3$ triplet (δ = 77.1), respectively. 1,3-Dimethyl-2-imidazolidinone (DMI) was dried over CaH_2. The nickel catalysts $NiCl_2(PPh_3)_2$, $NiCl_2$(dppf) were prepared according to the literature methods.[32,33] Boronate esters **1** with R = Ph, MeC_6H_4, $MeOC_6H_4$, 2-furyl, and (*E*)- and (*Z*)-$CH=CHC_5H_{11}$ were prepared by the literature procedures.[20,34] Organic extraction products were routinely dried over $MgSO_4$ and concentrated using a rotary evaporator to leave a residual oil, which was purified by chromatography on silica gel.

(*E*)-1-Pentyl-3-phenyl-2-propenyl Acetate (4a): A solution of (*E*)-1-phenyl-1-octen-3-ol (3.42 g, 16.8 mmol), pyridine (5.42 mL, 66.9 mmol), and Ac_2O (3.16 mL, 33.5 mmol) was stirred at room temperature overnight. Saturated $NaHCO_3$ and hexane were added to it, and the resulting mixture was stirred vigorously for 30 min. The aqueous layer was separated and extracted with hexane. The combined organic layers were dried and concentrated to leave an oil, which was purified by chromatography (hexane/EtOAc) to afford **4a** (3.74 g, 91%). − Bp: 130 °C (<0.1 Torr). − IR (neat): $\tilde{\nu}$ = 3028, 1738, 1240 cm^{-1}. − ^1H NMR: δ = 0.89 (t, *J* = 7 Hz, 3 H), 1.20−1.44 (m, 6 H), 1.56−1.82 (m, 2 H), 2.06 (s, 3 H), 5.40 (q, *J* = 7 Hz, 1 H), 6.12 (dd, *J* = 16, 7.5 Hz, 1 H), 6.60 (d, *J* = 16 Hz, 1

H), 7.20−7.39 (m, 5 H). − ^{13}C NMR: δ = 13.8, 21.1, 22.3, 24.6, 31.4, 34.3, 74.7, 126.5, 127.8, 128.5, 132.4, 136.4, 170.3. − $C_{16}H_{22}O_2$: calcd. C 78.01, H 9.00; found C 78.07, H 9.09.

(*E*)-1-Cyclohexyl-3-phenyl-2-propenyl Acetate (4b): An ethereal solution of *c*-$C_6H_{11}MgBr$ (5.1 mL, 1.18 M, 6.02 mmol) was diluted with Et_2O (5 mL) and *trans*-cinnamaldehyde (0.65 mL, 5.16 mmol) was added dropwise to the solution at 0 °C. After being stirred for 1 h, the solution was poured into saturated NH_4Cl. The mixture was extracted twice with EtOAc, and the combined extracts were dried and concentrated to leave an oil, which was purified by chromatography to furnish 1-cyclohexyl-3-phenyl-2-propen-1-ol (871 mg, 80%). − IR (neat): $\tilde{\nu}$ = 3392, 3026, 1449, 694 cm^{-1}. − ^{1}H NMR: δ = 0.96−1.96 (m, 12 H), 4.01 (t, *J* = 7 Hz, 1 H), 6.22 (dd, *J* = 16, 7 Hz, 1 H), 6.53 (d, *J* = 16 Hz, 1 H), 7.18−7.42 (m, 5 H).

A mixture of the above alcohol (256 mg, 1.18 mmol), Ac_2O (0.28 mL, 2.96 mmol), and pyridine (0.33 mL, 4.11 mmol) was stirred at room temperature for 5 h to afford **4b** (217 mg, 71%). − Bp: 190 °C (< 1 Torr). − IR (neat): $\tilde{\nu}$ = 3027, 1737, 1238, 750 cm^{-1}. − ^{1}H NMR: δ = 0.95−1.33 (m, 5 H), 1.56−1.86 (m, 6 H), 2.08 (s, 3 H), 5.21 (t, *J* = 8 Hz, 1 H), 6.11 (dd, *J* = 16, 8 Hz, 1 H), 6.57 (d, *J* = 16 Hz, 1 H), 7.21−7.41 (m, 5 H).

4,4-Ethylenedioxy-1-[(*E*)-2-phenylethenyl]butyl Acetate (4e): To an ice-cold solution of *trans*-cinnamaldehyde (0.67 mL, 5.31 mmol) in THF (15 ml) was added dropwise an ethereal solution of the Grignard reagent prepared from 3,3-ethylenedioxypropyl bromide (1.29 g, 7.13 mmol), Mg (260 mg, 10.8 mmol), 1,2-dibromoethane (a few drops), and THF (10 mL). After 1 h, saturated NH_4Cl was added and the mixture was extracted twice with EtOAc. The combined organic layers were dried and concentrated to afford a crude product, which was purified by chromatography (hexane/EtOAc) to afford (*E*)-6,6-ethylenedioxy-1-phenyl-1-hexen-3-ol (0.66 g, 53%). − IR (neat): $\tilde{\nu}$ = 3432, 3025, 1143 cm^{-1}. − ^{1}H NMR: δ = 1.71−1.89 (m, 4 H), 2.33 (br s, 1 H), 3.84−4.02 (m, 4 H), 4.34 (q, *J* = 6 Hz, 1 H), 4.93 (t, *J* = 4 Hz, 1 H), 6.22 (dd, *J* = 16, 6 Hz, 1 H), 6.60 (dd, *J* = 16, 1 Hz, 1 H), 7.20−7.40 (m, 5 H).

A mixture of the above alcohol (0.66 g, 2.82 mmol), Ac_2O (0.53 mL, 5.64 mmol), and pyridine (0.91 mL, 11.3 mmol) was stirred at room temperature overnight to afford **4e** (0.69 g, 89%) after a purification similar to that described above. − Bp: 220 °C (<1 Torr). − IR (neat): $\tilde{\nu}$ = 1736, 1714, 1240 cm^{-1}. − ^{1}H NMR: δ = 1.67−1.97 (m, 4 H), 2.08 (s, 3 H), 3.82−4.01 (m, 4 H), 4.91(t, *J* = 4 Hz, 1 H), 5.45 (q, *J* = 7 Hz, 1 H), 6.12 (dd, *J* = 16, 7.5 Hz, 1 H), 6.62 (d, *J* = 16 Hz, 1 H), 7.21−7.41 (m, 5 H). − ^{13}C NMR: δ = 21.2, 28.6, 29.4, 64.9, 74.3, 103.9, 126.7, 127.4, 128.0, 128.6, 132.8, 136.3, 170.5. − $C_{16}H_{20}O_4$: calcd. C 69.55, H 7.29; found C 69.24, H 7.21.

2-(4-Formylphenyl)-4,5-dimethyl-1,3,2-dioxaborolane (1d): To a solution of **13** (2.60 g, 14 mmol) in EtOH (28 mL) were added triethyl orthoformate (11.6 mL, 74 mmol) and *p*-TsOH·H_2O (20 mg, 0.11 mmol). The mixture was stirred at room temperature overnight and poured into saturated $NaHCO_3$. The resulting mixture was extracted twice with EtOAc. The combined organic layers were dried and concentrated to afford a crude product, which was purified by chromatography (hexane/EtOAc) to afford **15** (3.69 g, 89%). − ^{1}H NMR: δ = 1.23 (t, *J* = 7 Hz, 6 H), 3.46−3.66 (m, 4 H), 5.47 (s, 1 H), 7.36 (d, *J* = 9 Hz, 2 H), 7.94 (d, *J* = 9 Hz, 2 H).

To a solution of bromide **15** (3.79 g, 19.3 mmol) in THF (40 mL) was added *n*BuLi (8.8 mL, 2.3 M in hexane, 20.2 mmol) dropwise at −78 °C. After being stirred at −78 °C for 1 h, B(O-*i*Pr)$_3$ (4.90 mL, 21.2 mmol) was added to the solution. The resulting solution was gradually warmed to room temperature and then stirred overnight. Water (10 mL) and 3 N HCl (10 mL) were added and the resulting mixture was stirred at room temperature for 7 h vigorously. Brine was added to the mixture and the product was extracted with EtOAc twice.

To the combined extracts were added $MgSO_4$ and 2,3-butanediol (1.74 g, 19.4 mmol). The mixture was stirred at room temperature overnight and filtered through a pad of Celite. The filtrate was concentrated and the residue was purified by chromatography (hexane/EtOAc) to afford **1d** (3.90 g, 99%). − IR (neat): $\tilde{\nu}$ = 1711, 1375, 1093 cm^{-1}. − ^{1}H NMR: δ = 1.32 and 1.42 [2d (5:2), *J* = 6 and 6 Hz, 6 H], 4.19−4.27 and 4.67−4.81 [2m (2:5), 2 H], 7.88 (d, *J* = 8 Hz, 2 H), 7.98 (d, *J* = 8 Hz, 2 H), 10.06 (s, 1 H). − HRMS (EI) *m*/*z* calcd. for $C_{11}H_{13}BO_3$ (M^+) 204.0958; found 204.0957. − $C_{11}H_{13}BO_3$: calcd. C 64.75, H 6.42; found C 64.82, H 6.38.

2-(4-Acetylphenyl)-4,5-dimethyl-1,3,2-dioxaborolane (1e): In a manner similar to that described for the preparation of **1d**, 4-bromoacetophenone (**14**) was converted into the title compound. Briefly, **14** (4.61 g, 23.3 mmol), $HC(OEt)_3$ (19.3 mL, 116 mmol), *p*-TsOH·H_2O (44 mg, 0.23 mmol), and EtOH (13 mL) at 30 °C for 5 h afforded **16** (4.63 g, 72%). − ^{1}H NMR: δ = 1.20 (t, *J* = 7 Hz, 6 H), 1.52 (s, 3 H), 3.28−3.53 (m, 4 H), 7.38−7.50 (m, 4 H).

Acetal **16** (2.01 g, 7.20 mmol), *n*BuLi (3.60 mL, 2.4 M in hexane, 8.64 mmol), B(O-*i*Pr)$_3$ (1.99 mL, 8.64 mmol), and THF (30 mL) furnished the corresponding boronic acid **18** after hydrolysis with 1 N HCl (10 mL, room temperature, 1 h). A mixture of the boronic acid, 2,3-butanediol (0.65 mL, 7.2 mmol), and $MgSO_4$ (4 g) in EtOAc (40 mL) was stirred for 6 h to give **1e** (1.57 g, 100%). − IR (neat): $\tilde{\nu}$ = 1684, 1508, 1375 cm^{-1}. − ^{1}H NMR: δ = 1.31 (d, *J* = 6 Hz, 6 H), 2.63 (s, 3 H), 4.66−4.79 (m, 2 H), 7.86−7.96 (m, 4 H). − HRMS (EI) *m*/*z* calcd. for $C_{12}H_{15}BO_3$ (M^+) 218.1114; found 218.1121. − $C_{12}H_{15}BO_3$: calcd. C 66.10, H 6.93; found C 66.42, H 7.01.

2-[(4-Acetoxymethyl)phenyl]-4,5-dimethyl-1,3,2-dioxaborolane (1f): A solution of **19** (10.29 g, 55.0 mmol), DHP (5.52 mL, 60.5 mmol), and *p*-TsOH·H_2O (10 mg, 0.053 mmol) in CH_2Cl_2 (55 mL) was stirred at room temperature for 2 h and poured into saturated $NaHCO_3$. The resulting mixture was extracted with hexane twice. The combined hexane layers were dried and concentrated to afford a crude product, which was purified by chromatography (hexane/EtOAc) to give THP ether **20** (14.02 g, 94%). − IR (neat): $\tilde{\nu}$ = 1594, 1488 cm^{-1}. − ^{1}H NMR: δ = 1.45−1.94 (m, 6 H), 3.48−3.60 (m, 1 H), 3.83−3.96 (m, 1 H), 4.46 (d, *J* = 12 Hz, 1 H), 4.69 (t, *J* = 3.5 Hz, 1 H), 4.74 (d, *J* = 12 Hz, 1 H), 7.25 (d, *J* = 9 Hz, 2 H), 7.47 (d, *J* = 9 Hz, 2 H).

To a solution of bromide **20** (9.27 g, 34.19 mmol) in THF (100 mL) was added dropwise *n*BuLi (18.9 mL, 1.9 M in hexane, 35.9 mmol) at −78 °C and the solution was stirred at −78 °C for 1 h. To this was added B(O-*i*Pr)$_3$ (8.28 mL, 35.9 mmol) and the resulting solution was stirred overnight without new addition of dry ice to the cooling bath. Saturated NH_4Cl was added to the solution and the mixture was extracted twice with EtOAc. The combined extracts were dried and concentrated to afford crude 4-(tetrahydropyranyloxymethyl)phenylboronic acid (8.68 g).

A solution of the above boronic acid and *p*-TsOH·H_2O (290 mg, 1.5 mmol) in EtOH (20 mL) was stirred at room temperature for 4 h, and saturated $NaHCO_3$ was added. Volatile material was removed using a rotary evaporator, and the resulting mixture was extracted twice with EtOAc. The combined extracts were dried and concentrated to afford crude 4-(hydroxymethyl)phenylboronic acid. A mixture of this, Ac_2O (9.68 mL, 102 mmol), and pyridine (13.8 mL, 171 mmol) was stirred at room temperature overnight and poured into 3 N HCl. The combined extracts were washed with saturated $NaHCO_3$, dried, and concentrated to give **21** (6.09 g).

A mixture of **21**, 2,3-butanediol (3.11 g, 34.2 mmol), $MgSO_4$ (10 g), and Et_2O (30 mL) was stirred at room temperature overnight and filtered through a pad of Celite. The filtrate was concentrated and the residue was purified by chromatography to furnish **1f** (4.95 g, 58% from **20**). − IR (neat): $\tilde{\nu}$ = 1739, 1616, 1520, 1093 cm^{-1}. − ^1H NMR: δ = 1.30 and 1.40 [2d (5:1), *J* = 6 and 6 Hz, 6 H], 2.12 (s, 3 H), 4.15−4.23 and 4.65−4.77 [2 m, (1:5), 2 H], 5.13 (s, 2 H), 7.37 (d, *J* = 8 Hz, 2 H), 7.81 (d, *J* = 8 Hz, 2 H). − HRMS (EI) *m*/*z* calcd. for $C_{13}H_{17}BO_4$ (M^+) 248.1220; found 248.1221. − $C_{13}H_{17}BO_4$: calcd. C 62.94, H 6.91; found C 62.86, H 6.97.

2-[4-(3-Acetoxypropyl)phenyl]-4,5-dimethyl-1,3,2-dioxaborolane (1g): A solution of LDA in THF was prepared from *i*Pr_2NH (1.40 mL, 10 mmol), *n*BuLi (2.76 mmol, 2.72 M in hexane, 7.51 mmol), and THF (10 mL) at 0 °C for 15 min. *tert*-Butyl acetate (0.67 mL, 4.97 mmol) was added to it at −78 °C. The solution was warmed to −30 °C over 1 h and cooled again to −78 °C. DMSO (1.07 mL, 15.1 mmol) and a THF (5 mL) solution of **22** (1.00 g, 4.0 mmol) were added to the solution. The resulting solution was warmed to −30 °C over 1 h and poured into a mixture of hexane and saturated NH_4Cl. The phases were separated and the aqueous layer was extracted twice with hexane. The combined hexane solutions were dried and concentrated to give a residue, which was purified by chromatography (hexane/EtOAc) to furnish **23** (0.93 g, 82%). − IR (neat): $\tilde{\nu}$ = 1729, 1488, 1146 cm^{-1}. − ^1H NMR: δ = 1.41 (s, 9 H), 2.51 (t, *J* = 8 Hz, 2 H), 2.86 (t, *J* = 8 Hz, 2 H), 7.08 (d, *J* = 8 Hz, 2 H), 7.40 (d, *J* = 8 Hz, 2 H). − ^{13}C NMR: δ = 28.2, 30.6, 36.9, 80.6, 119.9, 130.1, 131.4, 139.7, 171.8. To an ice-cold solution of **23** (1.41 g, 4.94 mmol) in toluene (10 mL) was added DIBAL (13.8 mL, 1.0 M in toluene, 13.8 mmol). The solution was stirred at room temperature and poured slowly into an ice-cold mixture of Et_2O and 3 N HCl with vigorous stirring. After 30 min, the phases were separated and the aqueous layer was extracted with Et_2O. The combined extracts were washed with saturated $NaHCO_3$, dried, and concentrated. The residue was purified by chromatography (hexane/EtOAc) to afford **24** (0.95 g, 89%). − IR (neat): $\tilde{\nu}$ = 3341, 1488, 1071, 1011 cm^{-1}. − ^1H NMR: δ = 1.33 (br s, 1 H), 1.81−1.92 (m, 2 H), 2.67 (t, *J* = 8 Hz, 2 H), 3.66 (t, *J* = 6.5 Hz, 2 H), 7.07 (d, *J* = 9 Hz, 2 H), 7.40 (d, *J* = 9 Hz, 2 H). − ^{13}C NMR: δ = 31.4, 34.0, 62.0, 119.7, 130.4, 131.6, 140.9.
A solution of **24** (3.38 g, 15.7 mmol), DHP (1.58 mL, 17.3 mmol), and *p*-TsOH·H_2O (30 mg) in CH_2Cl_2 (16 mL) was stirred at room temperature for 5 h and poured with vigorous stirring into a mixture of hexane and saturated $NaHCO_3$. The phases were separated and the aqueous layer was extracted with hexane. The combined extracts were dried and concentrated to afford an oil, which was purified by chromatography (hexane/EtOAc) to furnish THP ether **25** (4.34 g, 92%). − IR (neat): $\tilde{\nu}$ = 1488, 1034 cm^{-1}. − ^1H NMR: δ = 1.42−1.95 (m, 8 H), 2.58−2.75 (m, 2 H), 3.34−3.55 (m, 2 H), 3.72−3.92 (m, 2 H), 4.55−4.59 (m, 1 H), 7.08 (d, *J* = 8 Hz, 2 H), 7.39 (d, *J* = 8 Hz, 2 H).
To a solution of the above compound **25** (4.15 g, 13.9 mmol) in THF (14 mL) was added dropwise *n*BuLi (5.35 mL, 2.7 M in hexane, 14.6 mmol) at −78 °C and the solution was stirred at −78 °C for 1 h. To this was added B(O-*i*$Pr)_3$ (3.20 mL, 13.9 mmol) and the resulting solution was stirred overnight without new addition of dry ice to the cooling bath. Saturated NH_4Cl was added to the solution and the mixture was extracted twice with EtOAc. The combined extracts were dried and concentrated to afford the corresponding boronic acid, which was used for the next reaction without purification.
A mixture of the boronic acid obtained above, MeOH, and 3 N HCl (a few drops) was stirred at room temperature for 3 h and poured into saturated $NaHCO_3$. The product was extracted twice with EtOAc. The combined extracts were dried and concentrated to afford crude 4-(3-hydroxypropyl)phenylboronic acid. A solution of the boronic acid, Ac_2O (2.62 mL, 27.6 mmol), and pyridine (4.49 mL, 55.6 mmol) was stirred at room temperature overnight and poured into 3 N HCl. The resulting mixture was extracted twice with EtOAc. The combined extracts were washed with saturated $NaHCO_3$, dried, and concentrated to give 4-(3-acetoxypropyl)-phenylboronic acid, which was esterified with 2,3-butanediol (1.26 mL, 13.9 mmol) in EtOAc in the presence of $MgSO_4$ to afford **1g** (1.93 g, 51% yield from **25**). − IR (neat): $\tilde{\nu}$ = 1739, 1612, 1095, 899 cm^{-1}. − ^1H NMR: δ = 1.29 and 1.39 [2d (2:1), *J* = 6 and 6 Hz, 6 H], 1.90−2.01 (m, 2 H), 2.05 (s, 3 H), 2.71 (dd, *J* = 8, 7 Hz, 2 H), 4.08 (t, *J* = 6 Hz, 2 H), 4.10−4.23 and 4.63−4.75 [2m (1:2), 2 H], 7.21 (d, *J* = 8 Hz, 2 H), 7.34 (d, *J* = 8 Hz, 2 H). − $C_{15}H_{21}BO_4$: calcd. C 65.24, H 7.66; found C 65.38, H 7.64.

(*E*)-2-(6-Acetoxy-1-hexenyl)-4,5-dimethyl-1,3,2-dioxaborolane (1h): To an ice-cold solution of BH_3·SMe_2 (0.60 mL, 2.0 M in THF, 1.2 mmol) was added (−)-α-pinene (0.48 mL, 3.0 mmol). The solution was stirred for 1 h at 0 °C and then for 2 h at room temperature to prepare (+)-$(Ipc)_2BH$. The solution was cooled down to −40 °C and acetylene **26** (103 mL, 0.735 mmol) was added. Stirring was continued for 1 h at −35 °C and then for 3 h at room temperature. Acetaldehyde (0.84 mL, 15 mmol) was added and the solution was gently refluxed for 12 h. Evaporation of the low-boiling materials afforded the corresponding diethyl boronate ester.
To a solution of the above product in THF (5 mL) was added 2,3-butanediol (0.10 mL, 1.1 mmol). After 3 h at room temperature, the solution was concentrated and the residue was purified by chromatography to afford **1h** (122 mg, 69%). − IR (neat): $\tilde{\nu}$ = 1739, 1639, 1371, 1244 cm^{-1}. − ^1H NMR: δ = 1.22 (d, *J* = 7 Hz, 6 H), 1.43−1.57 (m, 2 H), 1.57−1.72 (m, 2 H), 2.05 (s, 3 H), 2.16−2.25 (m, 2 H), 4.06 (t, *J* = 7 Hz, 2 H), 4.49−4.61 (m, 2 H), 5.47 (dt, *J* = 18, 1.5 Hz, 1 H), 6.63 (dt, *J* = 18, 6.5 Hz, 1 H). − $C_{12}H_{21}BO_4$: calcd. C 60.03, H 8.82; found 59.89, H, 8.61.

2-[4-(2-Ethoxycarbonylethyl)phenyl]-4,5-dimethyl-1,3,2-dioxaborolane (1i): To a suspension of LiCl (51 mg, 1.2 mmol) in MeCN (4 mL) were added triethyl phosphonoacetate (0.24 mL, 1.2 mmol), DBU (0.18 mL, 1.2 mmol), and aldehyde **1d** (204 mg, 1.00 mmol). The mixture was stirred at room temperature overnight and filtered through a pad of silica gel. The filtrate was concentrated to afford **27**. − ^1H NMR: δ = 1.34 (t, *J* = 7 Hz, 3 H), 1.40 (d, *J* = 6 Hz, 6 H), 4.13−4.25 (m, 2 H), 4.27 (q, *J* = 7 Hz, 2 H), 6.50 (d, *J* = 16 Hz, 1 H), 7.53 (d, *J* = 8 Hz, 2 H), 7.69 (d, *J* = 16 Hz, 1 H), 7.82 (d, *J* = 8 Hz, 2 H).
A mixture of **27**, 10% Pd/C (108 mg), and EtOH (10 mL) was stirred at room temperature overnight under hydrogen atmosphere and filtered through a pad of Celite. The filtrate was concentrated to afford the crude product, which upon chromatography (hexane/EtOAc) gave **1i** (221 mg, 80% yield from **1d**). − IR (neat): $\tilde{\nu}$ = 1736, 1095 cm^{-1}. − ^1H NMR: δ = 1.23 (t, *J* = 7 Hz, 3 H), 1.29 and 1.39 [2d (5:2), *J* = 6 and 6 Hz, 6 H], 2.62 (t, *J* = 8 Hz, 2 H), 2.97 (t, *J* = 8 Hz, 2 H), 4.12 (q, *J* = 7 Hz, 2 H), 4.13−4.21 and 4.63−4.75 [2m (2:5), 2 H], 7.23 (d, *J* = 8 Hz, 2 H), 7.74 (d, *J* = 8 Hz, 2 H). − HRMS (EI) *m*/*z* calcd. for $C_{15}H_{21}BO_4$ (M^+) 276.1533; found 276.1500. − $C_{15}H_{21}BO_4$: calcd. C 65.24, H 7.67; found C 65.15, H 7.69.

4,5-Dimethyl-2-[4-(3-oxobutyl)phenyl]-1,3,2-dioxaborolane (1j): To a mixture of dimethyl (2-oxopropyl)phosphonate (0.067 mL, 0.452 mmol), LiCl (19 mg, 0.448 mmol), and *i*Pr_2NEt (0.053 mL, 0.304 mmol) in MeCN (3.6 mL) was added aldehyde **1d** (61 mg, 0.299 mmol). The resulting mixture was stirred at room temperature overnight and poured into saturated NH_4Cl. The product was

extracted twice with EtOAc, and the combined extract was treated with 2,3-butanediol (0.030 mL, 0.33 mmol) and $MgSO_4$ (0.6 g) to convert the corresponding boronic acid, partially produced during the aqueous workup, into the ester. The mixture was filtered through celite with EtOAc and the filtrate was concentrated to give an oil, which was purified by chromatography to afford **28** (51 mg, 69%). − IR ($CHCl_3$): $\tilde{\nu}$ = 1665, 1608, 1093 cm^{-1}. − ^1H NMR: δ = 1.30 and 1.40 (2d, *J* = 6 and 6 Hz, 6 H), 2.39 (s, 3 H), 4.14−4.24 and 4.66−4.77 (2m, 2 H), 6.76 (d, *J* = 16 Hz, 1 H), 7.48−7.56 (m, 3 H), 7.83 (d, *J* = 8 Hz, 2 H).

Hydrogenation of **28** (1.22 g, 4.92 mmol) with 10% Pd/C (260 mg) and EtOAc (20 mL) under a hydrogen atmosphere at room temperature for 1 h afforded **1j** (936 mg, 77%) after purification by chromatography. − IR (neat): $\tilde{\nu}$ = 1716, 1612, 1095 cm^{-1}. − ^1H NMR: δ = 1.29 and 1.39 (2d, *J* = 6 and 6 Hz, 6 H), 2.14 (s, 3 H), 2.76 (t, *J* = 8 Hz, 2 H), 2.91 (t, *J* = 8 Hz, 2 H), 4.12−4.22 and 4.64−4.74 (2m, 2 H), 7.20 (d, *J* = 8 Hz, 2 H), 7.73 (d, *J* = 8 Hz, 2 H).

General Procedure for the Coupling Reaction: A flask was heated to melt commercial $ZnCl_2$ (86 mg, 0.63 mmol) under reduced pressure and flushed with argon. THF (3 ml) was added and the resulting mixture was cooled to 0 °C. To this, MeLi (0.618 mmol, 1.5−2 M in Et_2O) was added dropwise. The mixture was warmed up to room temperature over 15−30 min and boronate ester **1** (0.637 mmol) and DMI (0.21 mL, 1.92 mmol) were added to the solution. After 30−40 min, allylic acetate **3** (0.193 mmol) and $NiCl_2(PPh_3)_2$ (12 mg, 0.019 mmol) were added. The mixture was stirred at 40−50 °C for 8−12 h and poured into saturated NH_4Cl with vigorous stirring. The resulting mixture was extracted several times with hexane or EtOAc. The combined organic layers were dried and concentrated to afford a crude product, which was purified by chromatography (hexane/EtOAc) to afford the coupling product **5**. These results are summarized in Tables 3 and 4.

(*E*)-1,3-Diphenyl-1-octene (5a): 87% yield. The ^1H NMR spectrum was identical to that reported previously.[20]

(*E*)-3-(2-Methylphenyl)-1-phenyl-1-octene (5b): 89% yield. − IR (neat): $\tilde{\nu}$ = 3024, 1493, 1460 cm^{-1}. − ^1H NMR: δ = 0.87 (t, *J* = 6 Hz, 3 H), 1.20−1.46 (m, 6 H), 1.73−1.86 (m, 2 H), 2.36 (s, 3 H), 3.65 (q, *J* = 7 Hz, 1 H), 6.26 (dd, *J* = 16, 7 Hz, 1 H), 6.34 (d, *J* = 16 Hz, 1 H), 7.06−7.36 (m, 9 H). − ^{13}C NMR: δ = 14.0, 19.6, 22.5, 27.3, 31.8, 35.4, 44.2, 125.9, 126.2, 126.3, 126.5, 127.0, 128.5, 129.3, 130.5, 134.2, 135.9, 137.7, 142.8. − $C_{21}H_{26}$: calcd. C 90.59, H 9.41; found C 90.51, H 9.59.

(*E*)-3-(3-Methylphenyl)-1-phenyl-1-octene (5c): 81% yield. − IR (neat): $\tilde{\nu}$ = 3024, 1604, 962 cm^{-1}. − ^1H NMR: δ = 0.86 (t, *J* = 7 Hz, 3 H), 1.18−1.42 (m, 6 H), 1.71−1.83 (m, 2 H), 2.34 (s, 3 H), 3.35 (q, *J* = 7 Hz, 1 H), 6.31 (dd, *J* = 16, 7 Hz, 1 H), 6.39 (d, *J* = 16 Hz, 1 H), 6.98−7.38 (m, 9 H). − ^{13}C NMR: δ = 14.0, 21.4, 22.5, 27.2, 31.8, 35.8, 49.1, 124.7, 126.2, 126.9, 127.0, 128.43, 128.46, 128.5, 129.2, 134.7, 137.8, 138.1, 144.9. − $C_{21}H_{26}$: calcd. C 90.59, H 9.41; found C 90.39, H 9.23.

(*E*)-3-(4-Methylphenyl)-1-phenyl-1-octene (5d): 87% yield. − Bp: 220−230 °C (<1 Torr). − IR (neat): $\tilde{\nu}$ = 3024, 964 cm^{-1}. − ^1H NMR: δ = 0.86 (t, *J* = 7 Hz, 3 H), 1.17−1.40 (m, 6 H), 1.70−1.82 (m, 2 H), 2.32 (s, 3 H), 3.36 (q, *J* = 7 Hz, 1 H), 6.31 (dd, *J* = 16, 7 Hz, 1 H), 6.38 (d, *J* = 16 Hz, 1 H), 7.09−7.37 (m, 9 H). − ^{13}C NMR: δ = 14.0, 20.9, 22.5, 27.2, 31.8, 35.8, 48.7, 126.2, 127.0, 127.5, 128.5, 129.1, 129.2, 134.8, 135.7, 137.8, 141.8. − $C_{21}H_{26}$: calcd. C 90.59, H 9.41; found C 90.53, H 9.28.

(*E*)-3-(2-Methoxyphenyl)-1-phenyl-1-octene (5e): 88% yield. The ^1H NMR spectrum was identical to that reported previously.[20]

(*E*)-3-(4-Methoxyphenyl)-1-phenyl-1-octene (5f): 76% yield. The ^1H NMR spectrum was identical to that reported previously.[20]

(*E*)-3-(2-Furyl)-1-phenyl-1-octene (5g): 95% yield. The ^1H NMR spectrum was identical to that reported previously.[20]

(*E*)-3-Cyclohexyl-1,3-diphenyl-1-propene (5h): 94% yield. − IR (nujol): $\tilde{\nu}$ = 3022, 1597, 962 cm^{-1}. − ^1H NMR: δ = 0.76−1.98 (m, 11 H), 3.04−3.13 (m, 1 H), 6.360, 6.364, and 6.377 (3s, 2 H), 7.13−7.37 (m, 10 H).

(*E*)-3-Cyclohexyl-3-(2-methylphenyl)-1-phenyl-1-propene (5i): 82% yield. − IR (neat): $\tilde{\nu}$ = 3022, 1599, 962 cm^{-1}. − ^1H NMR: δ = 0.75−2.05 (m, 11 H), 2.36 (s, 3 H), 3.37 (t, *J* = 9 Hz, 1 H), 6.26 (dd, *J* = 16, 9 Hz, 1 H), 6.35 (d, *J* = 16 Hz, 1 H), 7.03−7.36 (m, 9 H).

(*E*)-3-Cyclohexyl-3-(4-methylphenyl)-1-phenyl-1-propene (5j): 87% yield. − IR (nujol): $\tilde{\nu}$ = 3024, 1599, 1512, 962 cm^{-1}. − ^1H NMR: δ = 0.76−1.96 (m, 11 H), 2.32 (s, 3 H), 2.98−3.13 (m, 1 H), 6.346, 6.349, and 6.362 (3s, 2 H), 7.05−7.37 (m, 9 H).

(*E*)-3-Cyclohexyl-3-(4-methoxyphenyl)-1-phenyl-1-propene (5k): 98% yield. − IR (nujol): $\tilde{\nu}$ = 1510, 1036, 960 cm^{-1}. − ^1H NMR: δ = 0.76−1.96 (m, 11 H), 3.01−3.08 (m, 1 H), 3.78 (s, 3 H), 6.333, 6.337, and 6.349 (3s, 2 H), 6.85 (d, *J* = 9 Hz, 2 H), 7.08−7.35 (m, 7 H).

(*E*)-1,3-Diphenyl-1-butene (5*l*): 83% yield. − IR (neat): $\tilde{\nu}$ = 1738, 1601, 1493, 1450 cm^{-1}. − ^1H NMR: δ = 1.46 (d, *J* = 7 Hz, 3 H), 3.58−3.69 (m, 1 H), 6.33−6.46 (m, 2 H), 7.15−7.38 (m, 10 H).

(*E*)-1,3,3-Triphenyl-1-propene (5m): 95% yield. − IR (nujol): $\tilde{\nu}$ = 1599, 742, 698 cm^{-1}. − ^1H NMR: δ = 4.90 (d, *J* = 8 Hz, 1 H), 6.35 (d, *J* = 16 Hz, 1 H), 6.68 (dd, *J* = 16, 8 Hz, 1 H), 7.18−7.42 (m, 15 H).

(*E*)-3-(4-Methoxyphenyl)-1,3-diphenylpropene (5n): 91% yield. − IR (neat): $\tilde{\nu}$ = 3026, 1510, 1250 cm^{-1}. − ^1H NMR: δ = 3.79 (s, 3 H), 4.85 (d, *J* = 8 Hz, 1 H), 6.32 (d, *J* = 16 Hz, 1 H), 6.65 (dd, *J* = 16, 8 Hz, 1 H), 6.85 (d, *J* = 8 Hz, 2 H), 7.12−7.39 (m, 12 H).

(1*E*,4*E*)-3-Pentyl-1-phenyl-1,4-decadiene (5o): 85% yield. − IR (neat): $\tilde{\nu}$ = 3082, 3059, 966 cm^{-1}. − ^1H NMR: δ = 0.84−0.93 (m, 6 H), 1.17−1.51 (m, 14 H), 1.96−2.06 (m, 2 H), 2.72−2.85 (m, 1 H), 5.35 (dd, *J* = 16, 7 Hz, 1 H), 5.44 (dt, *J* = 16, 7 Hz, 1 H), 6.11 (dd, *J* = 16, 7.5 Hz, 1 H), 6.33 (d, *J* = 16 Hz, 1 H), 7.14−7.38 (m, 5 H). − ^{13}C NMR: δ = 13.97, 13.99, 22.4, 22.5, 26.9, 29.1, 31.3, 31.8, 32.6, 35.2, 46.0, 126.1, 126.9, 128.5, 128.8, 130.6, 132.9, 134.5, 138.0. − $C_{21}H_{32}$: calcd. C 88.66, H 11.34; found C 88.57, H 11.04.

(1*E*,4*E*)-3-Cyclohexyl-1-phenyl-1,4-decadiene (5p): 81% yield. − IR (neat): $\tilde{\nu}$ = 3024, 1599, 746, 692 cm^{-1}. − ^1H NMR: δ = 0.86−1.81 (m, 20 H), 1.98−2.06 (m, 2 H), 2.56−2.64 (m, 1 H), 5.39−5.43 (m, 2 H), 6.15 (dd, *J* = 16, 8 Hz, 1 H), 6.31 (d, *J* = 16 Hz, 1 H), 7.15−7.38 (m, 5 H). − ^{13}C NMR: δ = 14.3, 22.7, 26.7, 26.8, 29.4, 30.9, 31.0, 31.6, 32.9, 42.6, 52.9, 126.0, 126.7, 128.4, 129.5, 131.2, 131.3, 133.0, 137.9.

(1*E*,4*Z*)-3-Pentyl-1-phenyl-1,4-decadiene (5q): 77% yield. − IR (neat): $\tilde{\nu}$ = 3082, 3059, 3024, 3001, 962 cm^{-1}. − ^1H NMR: δ = 0.84−0.92 (m, 6 H), 1.18−1.56 (m, 14 H), 2.02−2.12 (m, 2 H), 3.10−3.22 (m, 1 H), 5.25 (t, *J* = 11 Hz, 1 H), 5.45 (dt, *J* = 11, 7 Hz, 1 H), 6.10 (dd, *J* = 16, 7 Hz, 1 H), 6.34 (d, *J* = 16 Hz, 1 H), 7.14−7.38 (m, 5 H). − ^{13}C NMR: δ = 13.96, 13.99, 22.47, 22.55, 26.8, 27.5, 29.3, 31.5, 31.8, 35.6, 40.8, 126.1, 126.9, 128.4, 128.5, 130.3, 132.2, 134.2, 138.0. − $C_{21}H_{32}$: calcd. C 88.66, H 11.34; found C 88.69, H 11.21.

Methyl *trans*-5-Phenyl-3-cyclohexene-1-carboxylate (12): 86% yield. The ^{1}H NMR spectrum was identical with that reported.[6]

4-[(*E*)-1-Pentyl-3-phenyl-2-propenyl]benzaldehyde (5r): 75% yield. − IR (neat): $\tilde{\nu}$ = 3026, 1701, 1604 cm^{-1}. − ^{1}H NMR: δ = 0.86 (t, *J* = 7 Hz, 3 H), 1.18−1.39 (m, 6 H), 1.77−1.87 (m, 2 H), 3.50 (q, *J* = 8 Hz, 1 H), 6.30 (dd, *J* = 16, 8 Hz, 1 H), 6.42 (d, *J* = 16 Hz, 1 H), 7.17−7.45 (m, 7 H), 7.84 (d, *J* = 8 Hz, 2 H), 9.99 (s, 1 H). − ^{13}C NMR: δ = 14.3, 22.7, 27.4, 31.9, 35.9, 49.6, 126.2, 127.3, 128.3, 128.5, 130.1, 130.2, 133.0, 134.8, 137.2, 152.1, 191.9. − HRMS (EI) *m*/*z* calcd. for $C_{21}H_{24}O$ [M$^+$] 292.1827; found 292.1825.

4-[(*E*)-1-Cyclohexyl-3-phenyl-2-propenyl]benzaldehyde (5s): 89% yield. − IR (neat): $\tilde{\nu}$ = 3026, 1701, 1211 cm^{-1}. − ^{1}H NMR: δ = 0.78−1.99 (m, 11 H), 3.19 (t, *J* = 8 Hz, 1 H), 6.33 (dd, *J* = 16, 8 Hz, 1 H), 6.41 (d, *J* = 16 Hz, 1 H), 7.16−7.41 (m, 7 H), 7.83 (d, *J* = 8 Hz, 2 H), 9.97 (s, 1 H).

4-[(*E*)-1-Pentyl-3-phenyl-2-propenyl]acetophenone (5t): 87% yield. − IR (neat): $\tilde{\nu}$ = 3026, 1684, 1604, 1269 cm^{-1}. − ^{1}H NMR: δ = 0.86 (t, *J* = 7 Hz, 3 H), 1.14−1.42 (m, 6 H), 1.75−1.86 (m, 2 H), 2.59 (s, 3 H), 3.47 (q, *J* = 7 Hz, 1 H), 6.30 (dd, *J* = 16, 7 Hz, 1 H), 6.40 (d, *J* = 16 Hz, 1 H), 7.16−7.38 (m, 7 H), 7.92 (d, *J* = 8 Hz, 2 H). − ^{13}C NMR: δ = 13.9, 22.4, 26.5, 27.1, 31.7, 35.6, 49.1, 126.2, 127.3, 127.9, 128.6, 128.8, 130.1, 133.4, 135.4, 137.4, 150.6, 198.0. − HRMS (EI) *m*/*z* calcd. for $C_{22}H_{26}O$ [M$^+$] 306.1984; found 306.1982.

4-[4-((*E*)-1-Cyclohexyl-3-phenyl-2-propenyl)phenyl]-2-butanone (5u): 85% yield. − IR (neat): $\tilde{\nu}$ = 3008, 1714, 960 cm^{-1}. − ^{1}H NMR: δ = 0.76−1.95 (m, 11 H), 2.14 (s, 3 H), 2.69−2.90 (m, 4 H), 3.01−3.09 (m, 1 H), 6.335, 6.344, and 6.354 (3s, 2 H), 7.08−7.36 (m, 9 H).

4-[(*E*)-1-Pentyl-3-phenyl-2-propenyl]benzyl Acetate (5v): 89% yield. − IR (neat): $\tilde{\nu}$ = 3026, 1741, 1228 cm^{-1}. − ^{1}H NMR: δ = 0.86 (t, *J* = 6 Hz, 3 H), 1.14−1.42 (m, 6 H), 1.73−1.84 (m, 2 H), 2.09 (s, 3 H), 3.40 (q, *J* = 7 Hz, 1 H), 5.08 (s, 2 H), 6.29 (dd, *J* = 16, 7 Hz, 1 H), 6.39 (d, *J* = 16 Hz, 1 H), 7.14−7.38 (m, 9 H). − ^{13}C NMR: δ = 14.0, 21.0, 22.4, 27.2, 31.7, 35.7, 48.9, 66.2, 126.2, 127.1, 127.9, 128.5, 128.7, 129.5, 133.8, 134.3, 137.6, 145.1, 171.1. − $C_{23}H_{28}O_2$: calcd. C 82.10, H 8.39; found C 81.61, H 8.62.

3-[4-((*E*)-1-Pentyl-3-phenyl-2-propenyl)phenyl]propyl Acetate (5w): 83% yield. − IR (neat): $\tilde{\nu}$ = 3024, 1739, 1242 cm^{-1}. − ^{1}H NMR: δ = 0.86 (t, *J* = 7 Hz, 3 H), 1.16−1.40 (m, 6 H), 1.68−1.84 (m, 2 H), 1.86−2.04 (m, 2 H), 2.05 (s, 3 H), 2.59−2.67 (m, 2 H), 3.37 (q, *J* = 7 Hz, 1 H), 4.08 (t, *J* = 7 Hz, 2 H), 6.30 (dd, *J* = 16, 7 Hz, 1 H), 6.39 (d, *J* = 16 Hz, 1 H), 7.07−7.38 (m, 9 H). − ^{13}C NMR: δ = 14.0, 20.9, 22.4, 27.2, 30.0, 31.6, 31.7, 35.7, 48.7, 63.9, 126.2, 127.0, 127.7, 128.50, 128.54, 129.2, 134.7, 137.7, 139.0, 142.5, 171.3. − $C_{25}H_{32}O_2$: calcd. C 82.37, H 8.85; found C 81.89, H 8.90.

3-[4-((*E*)-1-Cyclohexyl-3-phenyl-2-propenyl)phenyl]propyl Acetate (5x): 92% yield. − IR (neat): $\tilde{\nu}$ = 3024, 1739, 1242 cm^{-1}. − ^{1}H NMR: δ = 0.76−2.08 (m, 16 H), 2.59−2.72 (m, 2 H), 3.02−3.10 (m, 1 H), 4.03−4.11 (m, 2 H), 6.341, 6.349, and 6.360 (3s, 2 H), 7.07−7.36 (m, 9 H).

Ethyl 3-[4-((*E*)-1-Pentyl-3-phenyl-2-propenyl)phenyl]propionate (5y): 95% yield. − IR (neat): $\tilde{\nu}$ = 3024, 1736, 1257 cm^{-1}. − ^{1}H NMR: δ = 0.86 (t, *J* = 7 Hz, 3 H), 1.16−1.40 (m, 9 H), 1.74−1.82 (m, 2 H), 2.60 (t, *J* = 8 Hz, 2 H), 2.92 (t, *J* = 8 Hz, 2 H), 3.37 (q, *J* = 7 Hz, 1 H), 4.13 (q, *J* = 7 Hz, 2 H), 6.30 (dd, *J* = 16, 7 Hz, 1 H), 6.38 (d, *J* = 16 Hz, 1 H), 7.11−7.40 (m, 9 H). − ^{13}C NMR: δ = 14.3, 14.4, 22.7, 27.5, 30.7, 32.0, 36.0, 36.1, 48.9, 60.5, 126.1, 127.0, 127.7, 128.38, 128.43, 129.1, 134.5, 137.6, 138.3, 142.6, 173.0. − HRMS (EI) *m*/*z* calcd. for $C_{25}H_{32}O_2$ [M$^+$] 323.1647; found 323.1642.

Ethyl 3-[4-((*E*)-1-Cyclohexyl-3-phenyl-2-propenyl)phenyl]propionate (5z): 84% yield. − IR (nujol): $\tilde{\nu}$ = 3024, 1736 cm^{-1}. − ^{1}H NMR: δ = 0.76−1.96 (m, 14 H), 2.60 (t, *J* = 8 Hz, 2H), 2.92 (t, *J* = 8 Hz, 2 H), 3.02−3.09 (m, 1 H), 4.11 (q, *J* = 7 Hz, 2 H), 6.26−6.41 (m, 2 H), 7.08−7.42 (m, 9 H).

(5*E*,8*E*)-7-Pentyl-9-phenyl-5,8-nonadienyl Acetate (5aa): 87% yield. − IR (neat): $\tilde{\nu}$ = 3024, 1739, 1240 cm^{-1}. − ^{1}H NMR: δ = 0.88 (t, *J* = 7 Hz, 3H), 1.21−1.70 (m, 12 H), 2.04 (s, 3 H), 2.01−2.10 (m, 2 H), 2.80 (m, 1 H), 4.06 (t, *J* = 7 Hz, 2 H), 5.38 (dd, *J* = 15, 6 Hz, 1 H), 5.44 (dt, *J* = 15, 6 Hz, 1 H), 6.10 (dd, *J* = 16, 8 Hz, 1 H), 6.34 (d, *J* = 16 Hz, 1 H), 7.15−7.39 (m, 5 H). − ^{13}C NMR: δ = 14.0, 20.9, 22.5, 25.7, 26.8, 28.0, 31.8, 32.1, 35.1, 46.0, 64.4, 126.1, 126.9, 128.5, 129.0, 129.7, 133.7, 134.3, 137.9, 171.4. − $C_{22}H_{32}O_2$: calcd. C 80.44, H 9.82; found C 80.70, H 9.81.

4-[(*E*)-1-((3,3-Ethylenedioxy)propyl)-3-phenyl-2-propenyl]benzaldehyde (5bb): 70% yield. − IR (neat): $\tilde{\nu}$ = 1698, 1604 cm^{-1}. − ^{1}H NMR: δ = 1.55−2.07 (m, 4 H), 3.54 (q, *J* = 8 Hz, 1 H), 3.81−3.99 (m, 4 H), 4.88 (t, *J* = 5 Hz, 1 H), 6.29 (dd, *J* = 16, 8 Hz, 1 H), 6.44 (d, *J* = 16 Hz, 1 H), 7.17−7.46 (m, 7 H), 7.84 (d, *J* = 8 Hz, 2 H), 9.98 (s, 1 H). − ^{13}C NMR: δ = 29.8, 32.0, 49.3, 65.0, 104.2, 126.2, 127.4, 128.3, 128.5, 130.2, 130.7, 132.3, 134.9, 137.0, 151.4, 191.8. − HRMS (CI) *m*/*z* calcd. for $C_{21}H_{23}O_3$ [M + H]$^+$ 323.1647; found 323.1642.

Reaction between Acetate 4a and MeZnCl: To an ice-cold mixture of $ZnCl_2$ (86 mg, 0.63 mmol) and THF (3 mL) was added MeLi (0.54 mL, 1.12 M in Et_2O, 0.605 mmol). The mixture was stirred at room temperature for 30 min, and **4a** (49 mg, 0.199 mmol) and $NiCl_2(PPh_3)_2$ (13 mg, 0.02 mmol) were added. The resulting mixture was stirred at 40−50 °C overnight and poured into saturated NH_4Cl with vigorous stirring. The resulting mixture was extracted twice with hexane. The combined organic layers were dried and concentrated to afford a crude product, which was purified by chromatography (hexane/EtOAc) to furnish methyl coupling product **10** (11 mg, 28%) and a 5:1 mixture of (1*E*,3*E*)- and (1*E*,3*Z*)-isomers of **9** (15 mg, 42%). Methyl coupling product **10**. − IR (neat): $\tilde{\nu}$ = 3026, 964, 746, 692 cm^{-1}. − ^{1}H NMR: δ = 0.88 (t, *J* = 7 Hz, 3 H), 1.07 (d, *J* = 7 Hz, 3 H), 1.20−1.42 (m, 8 H), 2.18−2.37 (m, 1 H), 6.09 (dd, *J* = 16, 8 Hz, 1 H), 6.33 (d, *J* = 16 Hz, 1 H), 7.15−7.39 (m, 5 H). − ^{13}C NMR: δ = 14.0, 20.6, 22.6, 27.0, 31.9, 37.0, 37.2, 126.0, 126.8, 128.0, 128.5, 137.2, 138.1. − $C_{15}H_{22}$: calcd. C 89.04, H 10.96; found C 88.91, H 10.87.

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