Construction of Terminal Conjugated Enynes: Regio- and Stereoselective Syntheses of 3-Alken-1-ynes and 1-Trimethylsilyl-3-alken-1-ynes from Alkenyldialkylboranes and (Trimethylsilyl)ethynyl Bromide

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Received 7 May 2002

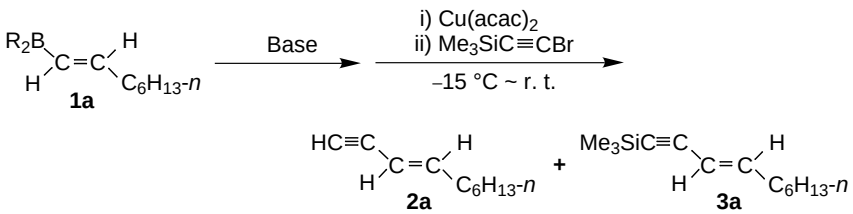
Abstract: The cross-coupling reaction of (*E*)- and (*Z*)-1-alkenyldialkylboranes with (trimethylsilyl)ethynyl bromide proceeds in the presence of a base and a catalytic amount of $Cu(acac)_2$ under very mild conditions to provide conjugated enynes whose carbon-carbon triple bond is in distal position. The use of 1 M NaOMe as a base exclusively affords both (*E*)- and (*Z*)-3-alken-1-ynes with high regio- and stereoselectivity, while the use of $LiOH·H_2O$ instead of 1 M NaOMe preferentially gives both (*E*)- and (*Z*)-1-trimethylsilyl-3-alken-1-ynes regio- and stereoselectively.

Key words: cross-coupling, 3-alken-1-yne, 1-trimethylsilyl-3-alken-1-yne, alkenyldialkylborane, (trimethylsilyl)ethynyl bromide

Conjugated enynes are valuable precursors to a variety of functionalized compounds such as polysubstituted benzenes via benzannulation reactions[1] and stereodefined conjugated dienes via semi-hydrogenation.[2] Furthermore, the enyne systems are found in a number of natural products such as laurencin[3] and neocarzinostatin chromophore.[4] Among conjugated enynes, there is a lively interest in 3-alken-1-yne due to its synthetic utility in which the acetylenic hydrogen can be converted into various functionalities including carbon-carbon bond formation. There have been several reports on the synthesis of 3-alken-1-yne using (trimethylsilyl)ethynyl halide as an ethynyl unit;[5–7] however, to the best of our knowledge, there are no reports of the combination of alkenylborane and (trimethylsilyl)ethynyl halide to afford 3-alken-1-yne. The cross-coupling reaction using organoboranes, i.e. Suzuki-Miyaura-type reaction,[8] requires base together with catalyst, while sp-hybridized carbon-silicon bond can be readily cleaved by basic methanolysis. Thus it was of interest to examine whether the cross-coupling reaction of alkenylboranes with (trimethylsilyl)ethynyl halide in the presence of base could proceed in a selective fashion to give the sole product. In this communication, we report a general and accessible route to both (*E*)- and (*Z*)-3-alken-1-ynes (**2** and **5**) as well as an analogous route to both (*E*)- and (*Z*)-1-trimethylsilyl-3-alken-1-ynes (**3** and **6**) using the cross-coupling reaction of (*E*)- and (*Z*)-1-alkenyldialkylboranes (**1** and **4**) with (trimethylsilyl)ethynyl bromide.

We examined the reaction of (*E*)-1-octenyldialkylborane (**1a**) with (trimethylsilyl)ethynyl bromide, prepared by bromination of (trimethylsilyl)ethyne with NBS, under various conditions. It was found that the reaction using $Cu(acac)_2$ as catalyst proceeded under very mild conditions to yield two products, (*E*)-3-decen-1-yne (**2a**) and (*E*)-1-trimethylsilyl-3-decen-1-yne (**3a**) (Scheme 1). The reaction was carried out using several bases, and the results are shown in Table 1. The ratio of **2a** to **3a** was dependent on base employed. Thus, the reaction using 1 M NaOMe gave **2a**[9] exclusively (entries 1, 8 and 9), while the reaction using $LiOH·H_2O$ gave **3a**[10] preferentially (entries 6 and 7). In addition, the use of 1.5 equivalents amount of **1a** increased the yield of the products (entries 7 and 9). It was also observed that the ratio and the yield of the products were affected by changing the dialkylboryl group of **1a** (entry 6 vs. 10 and entry 1 vs. 8).

Several types of (*E*)- and (*Z*)-1-alkenyldialkylboranes (**1** and **4**) were subjected to the reaction with (trimethylsilyl)ethynyl bromide under the conditions using two different bases, 1 M NaOMe and $LiOH·H_2O$. The results summarized in Table 2 and Scheme 2 revealed that the exclusive formation of **2** and **5** as well as the highly selective



Scheme 1

Synlett 2002, No. X, Print: xx xx xx.
Art Id.1437-2096,E;2002,0,MM,0001,0004,ftx,en;Y05402ST.pdf.

ISSN 0936-5214

Imprimatur:

Date, Signature

Table 1 Effect of Base and Bialkylborane[a]

Entry	R	Base	Yield of Products (%)[b]	
			2a	**3a**
1	*c*-C_6H_{11}	1 M NaOMe	66	Trace
2		2 M NaOH	56	2
3		*n*-BuLi	39	12
4		*t*-BuOK	15	14
5		CsF	21	1
6		$LiOH·H_2O$	2	50
7[c]			1	78
8	$(CH_3)_2CHCH(CH_3)$	1 M NaOMe	71	0
9[c]			75	0
10		$LiOH·H_2O$	17	53

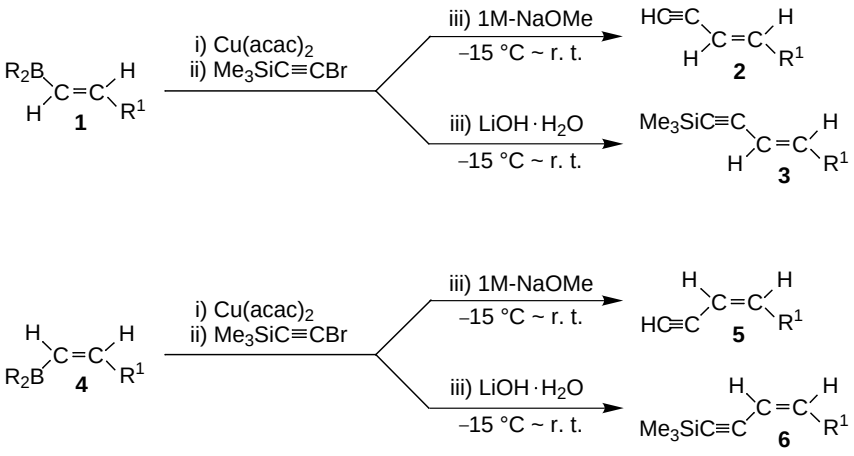
[a] Reactions were carried out at -15 °C to room temperature.
[b] GLC yields based on (trimethylsilyl)ethynyl bromide employed.
[c] 1.5 equivalents of (*E*)-1-octenyldialkylborane (**1**) was used.

formation of **3** and **6** was maintained completely or to a very similar extent in the cross-coupling reaction of **1** and **4** examined. The cross-coupling reaction of (*Z*)-1-octenyldialkylborane (**4a**), which was prepared by treatment of (*Z*)-1-iodo-1-octenyldialkylborane with $LiBEt_3H$,[11] proceeded under similar conditions to lead the selective formation of (*Z*)-3-decen-1-yne (**5a**)[12] (entry 2) and (*Z*)-1-trimethylsilyl-3-decen-1-yne (**6a**)[13] (entry 9) in the same manner as described in the reaction of **1a**. It should be noted that the presence of such functional groups as alkenyl, chloro and alkoxy in R^1 did not affect the present reaction at all. For the synthesis of **5** it is important to remove Et_3B liberated from $LiBEt_3H$ (entries 2 and 7). In the presence of Et_3B, for example, the cross-coupling reaction of **4a** using 1 M NaOMe decreased the yield of **5a** substantially, probably due to consumption of NaOMe by forming $NaBEt_3OMe$. In fact, further addition of NaOMe (2 equiv in total) restored the formation of **5a** to nearly the same yield. On the other hand, it is essential for the synthesis of **6a** to use DMF as co-solvent (entry 9). DMF appears to prevent interaction between **4a** and LiI generated in the step of the preparation of **4a**; indeed, the addition of LiI to **1a** decreased the yield of **3a** significantly. In the case where LiBr was generated, DMF was not required for the synthesis of (*Z*)-3-benzyloxy-1-trimethylsilyl-3-buten-1-yne (**6e**, entry 14).

Although we have no clear evidence for the reaction mechanism at present, the intermediate of the present reaction might be copper(III) species, as previously reported by Liebeskind et al[14] and Evans et al,[15] rather than simple alkenyl copper. Concerning the formation of 3-alken-1-yne, we believe that 1-trimethylsilyl-3-alken-1-yne would be formed at first even in the presence of 1 M NaOMe, and then the product would immediately undergo protodesilation with basic MeOH to produce 3-alken-1-yne.

The synthetic usefulness of 3-alken-1-yne thus prepared has been demonstrated by the palladium-copper catalyzed cross-coupling reaction with aryl halide (Sonogashira reaction).[16] For example, in the presence of aq tetrabutylammonium hydroxide[17] the reaction of **2a** and **5a** with iodobenzene using catalytic amounts of $PdCl_2(PPh_3)_2$ and CuI proceeded smoothly at room temperature to provide (*E*)- and (*Z*)-1-phenyl-3-decen-1-yne,[18] respectively, in good overall yields in a one-pot manner from the preparation of bis(1,2-dimethylpropyl)borane (Scheme 3).

In summary, we have developed a highly flexible protocol that allows the synthesis of (*E*)- and (*Z*)-3-alken-1-yne (**2** and **5**) with protodesilation as well as the synthesis of (*E*)- and (*Z*)-1-trimethylsilyl-3-alken-1-yne (**3** and **6**) without protodesilation. As shown in Scheme 3, successive coupling reaction of (*E*)- and (*Z*)-1-alkenyl group with two distinct electrophiles without isolation of any intermediates will provide a new synthetic route for linear conjugated compounds possessing an enyne unit. Further studies on the scope and synthetic application of the present reaction are currently under investigation in our laboratory.

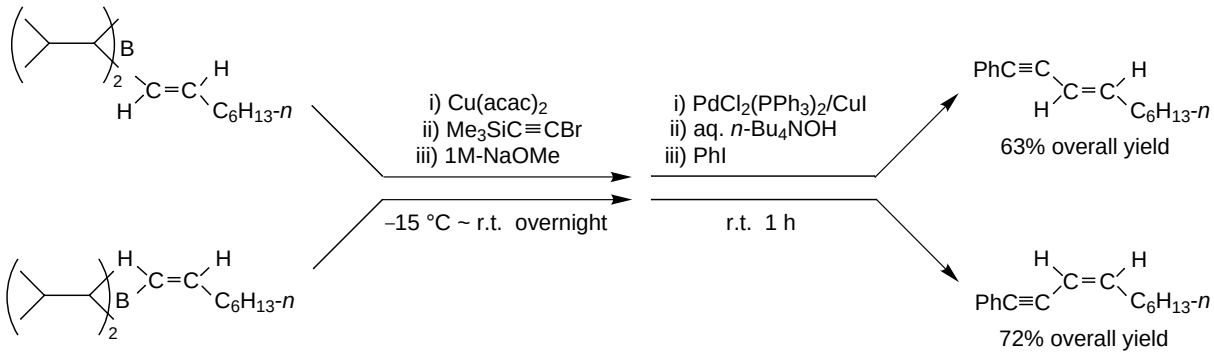


Scheme 2

Table 2 $Cu(acac)_2$-Catalyzed Cross-Coupling Reaction of *(E)*- and *(Z)*-1-Alkenyldialkylboranes with (Trimethylsilyl)ethynyl Bromide[a]

Entry	R	Base	R^1	Yield of Products (%)[b]				
					2	**3**	**5**	**6**
1	$(CH_3)_2CHCH(CH_3)$	1 M NaOMe	*n*-C_6H_{13}	(**a**)	70	0		
2[c]				(**a**)			75	0
3			C_6H_5	(**b**)	70	0		
4				(**c**)	63	0		
5			$Cl(CH_2)_3$	(**d**)	67	0		
6			$C_6H_5CH_2OCH_2$	(**e**)	74	0		
7[c,d]				(**e**)			60	0
8	*c*-C_6H_{11}	$LiOH·H_2O$	*n*-C_6H_{13}	(**a**)	1	72		
9[e]				(**a**)			3	49
10			C_6H_5	(**b**)	3	73		
11				(**c**)	1	62		
12			$Cl(CH_2)_3$	(**d**)	Trace	72		
13			$C_6H_5CH_2OCH_2$	(**e**)	4	63		
14[d]				(**e**)			Trace	66

[a] Unless otherwise specified, reaction of 1-alkenyldialkylborane (1.5 equiv) with (trimethylsilyl)ethynyl bromide (1 equiv) was carried out in THF at -15 °C to room temperature.
[b] Isolated yield based on (trimethylsilyl)ethynyl bromide employed.
[c] After removal of Et_3B, formed by treatment with $LiBEt_3H$, under reduced pressure, the residue was dissolved in THF and then the solution was subjected to the cross-coupling reaction.
[d] (*Z*)-3-Benzyloxy-1-propenyldialkylborane was prepared from 3-benzyloxy-1-bromo-1-propyne.
[e] DMF was used as co-solvent in the cross-coupling step.



Scheme 3

Acknowledgement

The present research is supported by Grant-in-Aid for Scientific Research (C) from The Ministry of Education, Science, Sports and Culture, Japan.

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(9) To a stirred solution of (*E*)-1-octenylbis(1,2-dimethylpropyl)borane (4 mmol) in THF (12 mL) at -15 °C, $Cu(acac)_2$ (0.052 g, 0.2 mmol) was added under an argon flow. (Trimethylsilyl)ethynyl bromide (0.474 g, 2.68 mmol) and 1 M NaOMe (4 mL, 4 mmol) were then added dropwise to the solution, and the resulting mixture was allowed to warm gradually to room temperature and to stir overnight. The reaction mixture was treated with 3 M NaOH (4 mL) and 30% H_2O_2 (2 mL) at 0 °C and stirred for 1 h at the same temperature to decompose the residual organoboron compound. The resultant mixture was extracted with ether, washed with brine, and dried over anhydrous Na_2SO_4. The solvent was removed on a rotary evaporator under reduced pressure, and the crude product was purified by column chromatography on silica gel, with *n*-pentane as eluent, to give product **2a** (0.255 g, 70% yield) as a colorless liquid. Compound **2a**: ^{1}H NMR ($CDCl_3$) δ: 0.88 (t, 3 H), 1.1–1.5 (m, 8 H), 2.0–2.2 (m, 2 H), 2.76 (dd, *J* = 2.2, 0.4 Hz, 1 H), 5.47 (ddt, *J* = 16.0, 2.2, 1.5 Hz, 1 H), 6.22 (dtd, *J* = 16.0, 6.8, 0.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ: 14.04, 22.60, 28.58, 28.79, 31.68, 33.02, 75.49 (CH), 82.66 (C–), 108.52 (=CH–), 146.96 (=CH–); IR(neat) 3315, 3024, 2956, 2927, 2856, 2104, 1629, 1465, 1436, 954, cm^{-1}; HRMS (EI) $C_{10}H_{16}$: requires 136.1252; found 136.1254.
(10) To a stirred solution of (*E*)-1-octenyldicyclohexylborane (4 mmol) in THF (12 mL) at -15 °C, $Cu(acac)_2$ (0.052 g, 0.2 mmol) was added under an argon flow. (Trimethylsilyl)ethynyl bromide (0.474 g, 2.68 mmol) was added dropwise to the solution, and then $LiOH·H_2O$ (0.168 g, 4 mmol) was introduced into the solution under an argon flow. The resulting mixture was allowed to warm gradually to room temperature and to stir overnight. After the reaction mixture was neutralized with sat. NH_4Cl, the resultant mixture was treated with $NaBO_3·4H_2O$ (1.846 g, 12 mmol) and H_2O (4 mL) at room temperature with vigorous stirring for 2 h to decompose the residual organoboron compound. Workup is the same as described in ref.[9]. The crude product was purified by column chromatography on silica gel, with *n*-pentane as eluent, to give product **3a** (0.401 g, 72% yield) as a colorless liquid. Compound **3a**: ^{1}H NMR ($CDCl_3$) δ: 0.17 (s, 9 H), 0.88 (t, 3 H), 1.1–1.5 (m, 8 H), 2.0–2.2 (m, 2 H), 5.52 (dt, *J* = 15.8, 1.5 Hz, 1 H), 6.20 (dt, *J* = 15.8, 6.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 0.00 (Me × 3), 14.00, 22.55, 28.58, 28.78, 31.63, 33.06, 92.43 (C–), 104.28 (C–), 109.61 (=CH–), 146.26 (=CH–); IR(neat) 2958, 2927, 2856, 2175, 2133, 1249, 1085, 952, 842, 759 cm^{-1}; HRMS (EI) $C_{13}H_{24}Si$: requires 208.1647, found 208.1664.
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(12) (*Z*)-3-Decen-1-yne(**5a**): ^{1}H NMR ($CDCl_3$) δ: 0.88 (t, 3 H), 1.1–1.55 (m, 8 H), 2.2–2.45 (m, 2 H), 3.05 (d, *J* = 2.2 Hz, 1 H), 5.45 (ddt, *J* = 11.0, 1.3, 0.9 Hz, 1 H), 5.98 (dtd, *J* = 11.0, 7.3, 0.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.04, 22.60, 28.74, 28.87, 30.29, 31.68, 80.62 (C–), 81.11 (CH), 108.03 (=CH–), 146.22 (=CH–); IR(neat) 3313, 3024, 2956, 2927, 2856, 2358, 1465, 738 cm^{-1}; HRMS (EI) $C_{10}H_{16}$: requires 136.1252, found 136.1253.
(13) (*Z*)-1-Trimethylsilyl-3-decen-1-yne(**6a**): ^{1}H NMR ($CDCl_3$) δ 0.19 (s, 9 H), 0.88 (t, 3 H), 1.1–1.55 (m, 8 H), 2.2–2.45 (m, 2 H), 5.48 (dt, *J* = 11.0, 1.3 Hz, 1 H), 5.94 (dt, *J* = 11.0, 7.3 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 0.00 (Me × 3), 14.00, 22.59, 28.66, 28.78, 30.25, 31.59, 98.41 (C–), 102.24 (C–), 109.16 (=CH–), 145.57 (=CH–); IR(neat) 3020, 2958, 2927, 2856, 2148, 1249, 842, 759 cm^{-1}; HRMS (EI) $C_{13}H_{24}Si$: requires 208.1647, found 208.1671.
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(18) (*E*)-1-Phenyl-3-decen-1-yne: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 3 H), 1.1–1.5 (m, 8 H), 2.05–2.3 (m, 2 H), 5.70 (dt, *J* = 15.8, 1.4 Hz, 1 H), 6.22 (dt, *J* = 15.8, 7.0 Hz, 1 H), 7.2–7.5 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ: 14.04, 22.60, 28.79(–CH_2– × 2), 31.68, 33.22, 87.91 (C–), 88.44 (C–), 109.57 (=CH–), 123.79 (=C<), 127.82 (=CH–), 128.22 (=CH– × 2), 131.44 (=CH– × 2), 145.16 (=CH–); IR(neat) 3080, 3055, 3020, 2954, 2927, 2854, 2202, 1596, 1571, 1488, 1463, 1454, 1442, 1379, 1303, 1068, 952, 912, 754, 690 cm^{-1}; MS (EI) *m/z* 212 (M^+, 51%), 183(3), 169(6), 155(24), 141(78), 128(100), 115(41), 102(6), 91(13), 77(7), 63(4). (*Z*)-1-Phenyl-3-decen-1-yne: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 3 H), 1.1–1.5 (m, 8 H), 2.25–2.55 (m, 2 H), 5.67 (dt, *J* = 10.8, 1.1 Hz, 1 H), 5.96 (dt, *J* = 10.8, 7.0 Hz, 1 H), 7.2–7.5 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 14.08, 22.64, 28.87(–CH_2– × 2), 30.41, 31.72, 86.57 (C–), 93.45 (C–), 109.05 (=CH–), 123.87 (=C<), 127.94 (=CH–), 128.27 (=CH– × 2), 131.40 (=CH– × 2), 144.31 (=CH–); IR(neat) 3080, 3058, 3020, 2956, 2927, 2856, 1595, 1571, 1488, 1467, 1456, 1440, 1398, 1377, 1068, 1028, 1014, 912, 754, 732, 690 cm^{-1}; HRMS (EI) $C_{16}H_{20}$: requires 212.1565, found 212.1559.