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Intramolecular cyanoboration of alkynes via activation of boron–cyanide bonds by transition metal catalysts

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Abstract

Cyano(dialkylamino)boryl ethers of homopropargylic alcohols undergo intramolecular addition of a B–CN bond across their carbon–carbon triple bonds (cyanoboration) in the presence of palladium and nickel catalysts, furnishing five-membered cyclic boryl ethers regioselectively in good yields via 5-exo cyclization. The products were transformed into highly substituted α,β-unsaturated nitriles via Suzuki–Miyaura coupling to aryl iodides, rhodium-catalyzed conjugative addition to methyl vinyl ketone, and rhodium-catalyzed protodeborylation.

Keywords: Borylation; Cyanation; Cyanoborane; Addition; Palladium; Nickel

1. Introduction

Transition metal-catalyzed addition of σ-bonds across carbon–carbon multiple bonds is an important process used in organic synthesis. Recent attention has focused on the activation and addition of σ-bonds between elements other than hydrogen [1], because such additions can lead to the development of efficient multiple functionalizations of organic molecules. The multifunctionalized molecules thus produced can serve as useful synthetic intermediates in organic synthesis, so in the development of synthetically useful processes, it is important to explore new addition reactions of σ-bonds between groups of high synthetic utility.

We have been involved in the development and synthetic applications of additions of silicon- and boron-containing σ-bonds, such as Si–Si [2] and Si–B [3] bonds, across carbon–carbon multiple bonds. In particular, Si–B bonds exhibit high reactivities in addition reactions, enabling highly regio- and stereoselective silaboration reactions using nickel, palladium, and platinum catalysts. In the silaboration of allenes, for example, highly enantioface-selective asymmetric silaboration has been achieved by using a well-tuned catalyst system bearing optically active monophosphine ligands on palladium [4]. Furthermore, double insertion reactions involving the activation of Si–B bonds have also been developed, leading to the concomitant formations of C–C and B–C bonds with either Si–O or Si–C bonds [5]. The development of a series of silaboration reactions led us to believe that an exploration of boron compounds that undergo addition reactions across unsaturated organic compounds will open up new pathways to organoboron compounds that would otherwise be inaccessible.

Our attention focused on carboboration, where C–C and B–C bonds are created simultaneously. We were interested in the reactivity of cyanoboranes [6] in such addition reactions using transition metal catalysts. Although no synthetic application had appeared for long time since their first syntheses in 1959 [6,7], we have

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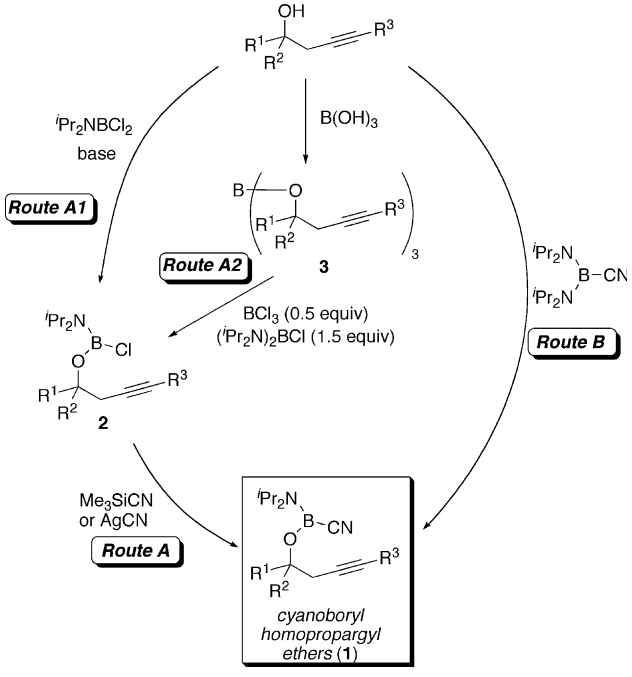
recently succeeded in using bis(amino)cyanoborane in a Strecker-type reaction for the efficient synthesis of α-amino nitriles [8].

Our initial efforts on the intermolecular cyanoboration of alkynes using cyanoboranes, however, all failed. The failure urged us to reevaluate our hypothesis that boron–cyano bonds would be activated by transition metal catalysts.

We decided to examine the possibility of B–CN bond activation by means of an intramolecular reaction, because the facile capture of the alkyne moiety by the activated cyanoborane is anticipated for the intramolecular variants. Indeed, an intramolecular reaction seems to be a good measure of B–CN bond activation by a transition metal catalyst. As previously reported [9], such an intramolecular cyanoboration reaction turned out to be successful. In this paper, we summarize the details of the intramolecular cyanoboration of alkynes. We have found that palladium and nickel complexes are able to activate B–CN bonds, leading to an addition reaction to carbon–carbon triple bonds.

2. Preparation of cyanoboryl ethers of homopropargylic alcohols

Cyanoboryl ethers **1** of homopropargylic alcohols that bear a dialkylamino group on the boron atom were chosen as substrates for the intramolecular cyanoboration (Scheme 1). The presence of the amino group on the boron atom is crucial for the stabilization of the



Scheme 1. Synthetic accesses to cyanoborl ethers of homopropargylic alcohols **1**.

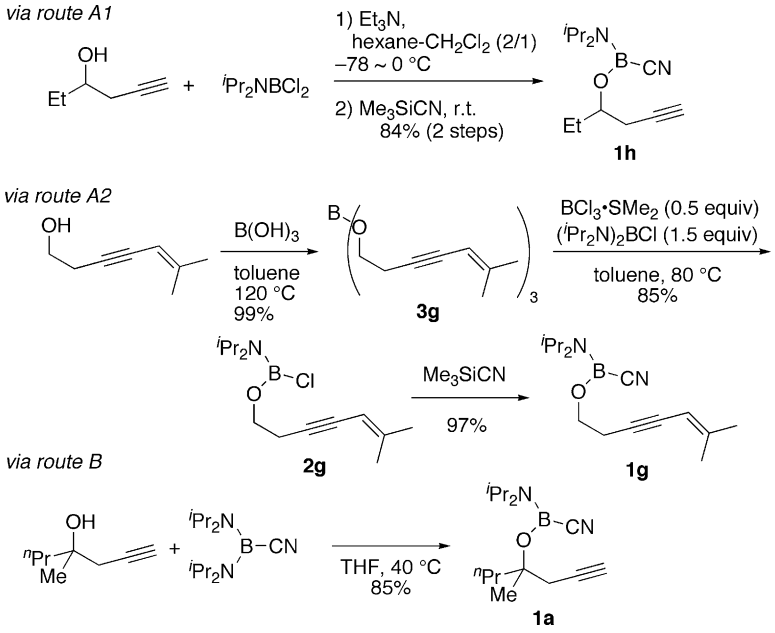
cyanoborane derivatives. There are two major synthetic routes to form the cyanoboryl ethers. The first route involves a chloro-cyano exchange on the boron atom in the final step (Route A) [6a,6d]. The chloro–cyano exchange reaction is achieved by reacting the chloroboranes with silver cyanide or trimethylsilyl cyanide. The required chloroboranes **2** were prepared either by reaction of dichloro(diisopropylamino)borane with homopropargylic alcohols in the presence of triethylamine (Route A1) or by the redistribution of tris(homopropargyloxy)borane **3** with trichloroborane and chlorobis(diisopropylamino)borane (Route A2). The former chloroborane synthesis and the subsequent chloro-cyanide exchange reaction were carried out in one-pot reaction.

The second synthetic route to form cyanoboryl ethers involves an amino-alkoxy exchange reaction of bis(diisopropylamino)cyanoborane with homopropargylic alcohols (Route B). It is of interest to note that the amino-alkoxy exchange takes place favorably over cyano-alkoxy exchange. Indeed, no loss of the cyano group was observed in the reaction of bis(diisopropylamino)cyanoborane with homopropargylic alcohols. Although Route B can be regarded as being the most convenient method to prepare functionalized cyanoboranes, the method can only be applied to tertiary homopropargylic alcohols. If secondary and primary alcohols are used, then a non-selective exchange reaction takes place, leading to the formation of trialkoxyboron derivatives in significant quantities. Therefore, Route A1 or A2 should be used for these alcohols.

Representative synthesis of cyanoboryl ethers of homopropargylic alcohols are shown in Scheme 2. The synthesis of the cyanoboryl ether **1h** of *sec*-homopropargylic alcohol was accomplished in an 84% yield via Route A1. The cyanoboryl ether **1g** was synthesized from trialkoxyborane **3g**, which was synthesized from the corresponding enynol in a high yield. The trialkoxyborane **3g** was treated with a borontrichloride dimethylsulfide complex and chlorobis(diisopropylamino)borane at 80 °C, affording the chloro(alkoxy)-(diisopropylamino)borane **2g** in an 85% yield. The chloroborane **2g** was converted into the corresponding cyanoborane **1g** in a high yield. On the other hand, cyanoboryl ethers **1a**–**1d** were prepared via Route B in high yields from tertiary homopropargylic alcohols. The cyanoboryl ethers were isolated by distillation for subsequent use in the intramolecular reactions.

3. Intramolecular cyanoboration of alkynes

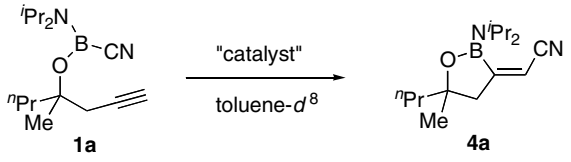
On the successful synthesis of cyanoboryl ethers, we began to determine the suitable reaction conditions for intramolecular cyanoboration. A success in intramolecular cyanosilylation [10] led us to investigate palladium



Scheme 2. Representative synthesis of cyanoboryl ethers of homopropargyl alcohols.

catalysts for cyanoboration. In the presence of divalent palladium salts, such as $Pd(acac)_2$ and $PdCl_2$, cyanoboryl ether **1a** underwent intramolecular cyanoboration at 110 °C, affording the five-membered cyclic boryl ether **4a** in good yield (Table 1, Entries 1 and 2). It should be noted here that the cyanoboration proceeded with high regio- and stereoselectivity, leading to the exclusive formation of a *cis*-addition product that was formed through a formal 5-exo cyclization. We found that the cyclization proceeded even at 80 °C, albeit in a moderate yield, in the presence of pyridine (2.0 equiv to Pd) with $PdCl_2$, which has been reported as the best catalyst combination for use in the intermolecular cyanosilylation (Entry 3) [11]. The use of an acetonitrile complex of palladium chloride also allowed the reaction to proceed at 80 °C in a good yield (Entry 4), even though the use of bis(triphenylphosphine)palladium(II) chloride was totally ineffective (Entry 5).

Table 1
Catalyst screening for the intramolecular cyanoboration of **1a**[a]

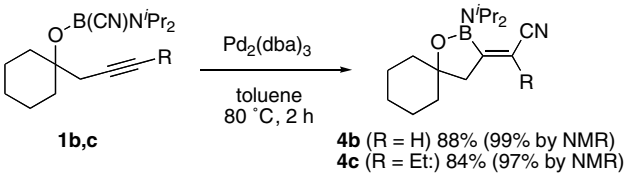


Entry	Catalyst	%Yield (reaction time)[b]		
		At 50 °C	At 80 °C	At 110 °C
1	$Pd(acac)_2$	nr	nr	86 (8 h)
2	$PdCl_2$	nr	nr	83 (8 h)
3	$PdCl_2$-pyridine	nr	71 (3 h)	–
4	$PdCl_2(MeCN)_2$	nr	94 (5 h)	–
5	$PdCl_2(PPh_3)_2$	nr	nr	nr
6	PdCp(π-allyl)	nr	91 (2 h)	–
7	$Pd(PPh_3)_4$	38 (96h)	70 (14 h)	74 (1 h)
8	$Pd_2(dba)_3$	94 (18 h)	98 (2 h)	–
9	$Ni(COD)_2$	13 (96 h)	80 (96 h)	93 (2 h)

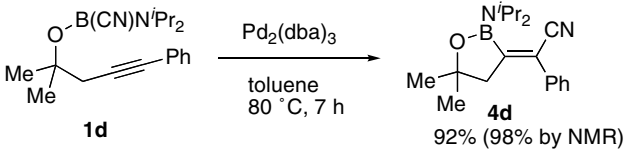
[a] Cyanoborane **1a** (0.30 mmol) in toluene-d_8 (0.5 mL) was stirred in the presence of the palladium or nickel complexes (5 mol% Pd or Ni).
[b] NMR yield (1,3-dimethoxybenzene as an internal standard). Abbreviations: nr, no reaction for 3 h; –, reactions not carried out.

Cyclopentadienyl(π-allyl)palladium(II), a convenient divalent precursor for zero-valent palladium complexes, also served as a good catalyst for the intramolecular cyanoboration of **1a** (Entry 6). The screening of these catalysts also finally led us to consider zero-valent palladium complexes, such as $Pd(PPh_3)_4$ and $Pd_2(dba)_3$, as the most active palladium catalysts (Entries 7 and 8). They afforded the cyclization product even at 50 °C; in particular, the $Pd_2(dba)_3$ complex gave the cyanoboration product in a high yield at 50 °C within a period of 18 h. It is important to note that a nickel complex also served as an effective catalyst for intramolecular cyanoboration, indicating that activation of the boron–cyanide bond is effected by nickel as well as by palladium (Entry 9).

We then focused our attention on the scope of the cyanoboration reaction. Cyanoboryl ethers **1b** and **1c** prepared from 1-propargylcyclohexanols underwent cyclization in high yields in the presence of $Pd_2(dba)_3$, regardless of the substituents at the *SP* carbon atoms (Eq. (1)). No significant difference in the reaction rate was noticeable in these reactions. Similarly, the phenyl-substituted alkynyl group successfully took part in the cyanoboration (Eq. (2)).

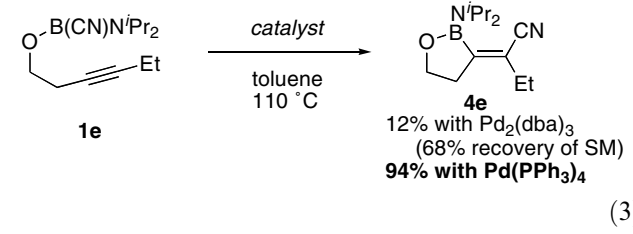


(1)



(2)

The reaction of cyanoboryl ethers derived from *prim*-homopropargylic alcohols, however, did not work well in the presence of $Pd_2(dba)_3$. The reaction of **1e** under the optimum reaction conditions for the tertiary homopropargylic ethers resulted in only 12% yield, along with the recovery of the starting material (68%) (Eq. (3)). We found that the use of tetrakis(triphenylphosphine)palladium(0) as a catalyst markedly improved the reaction yield to 94% at 110 °C. These modified reaction conditions were suitable for the intramolecular cyanoboration of **1f** and **1g**, which were derived from *prim*- and *sec*-homopropargylic alcohols with internal carbon–carbon triple bonds (Eqs. (4) and (5)).



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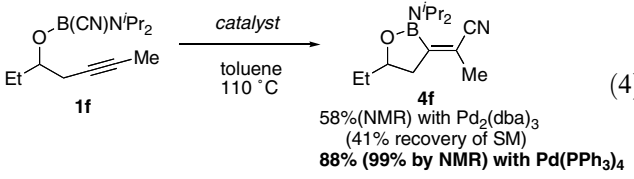

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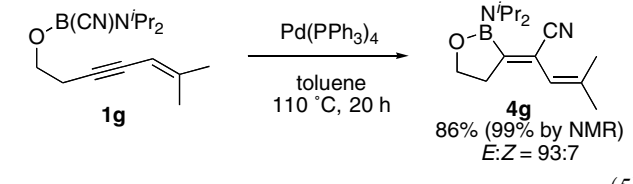
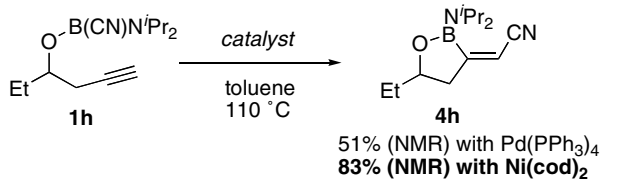


(5)

A nickel catalyst was found to be more effective than a palladium catlayst in the cyanoboration reactions of terminal alkynes derived from *prim*- and *sec*-homopropargylic alcohols. For example, the reaction of **1h** in the presence of a catalytic quantity of $Ni(cod)_2$ afforded the corresponding cyanoboration product **4h** in an 83% yield, whereas the $Pd(PPh_3)_4$ catalyst gave the same product in only a 51% yield under otherwise the same reaction conditions (Eq. (6)). A similar tendency was also found in the reactions of **1i** (58% yield vs. 45% yield using $Ni(cod)_2$ and $Pd(PPh_3)_4$, respectively) (Eq. (7)).



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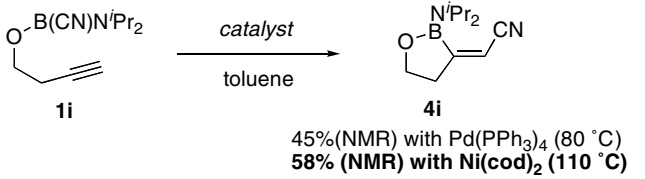
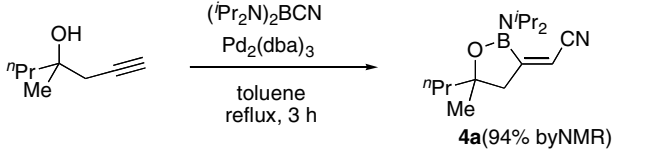


(7)

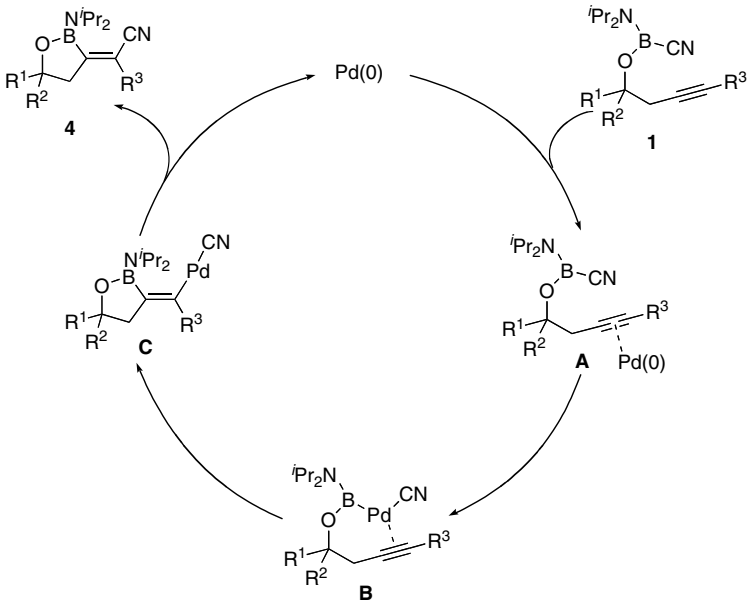
This optimization study led us to establish the following guidelines in choosing a suitable catalyst for intramolecular cyanoboration reactions: (1) $Pd_2(dba)_3$ is the best catalyst for cyanoboryl ethers of *tert*-homopropargylic alcohols; (2) the use of $Pd(PPh_3)_4$ is preferable for *internal* alkynes that are derived from *prim*- and *sec*-homopropargylic ethers; and (3) $Ni(cod)_2$ gives the highest yields for *terminal* alkynes derived from *prim*- and *sec*-homopropargylic ethers.

All the intramolecular cyanoboration reactions shown thus far were carried out using isolated cyanoboryl ethers. In certain cases, where the cyanoboryl ethers can be prepared via amino-alkoxy exchange (Route B), a one-pot intramolecular cyanoboration can be applied to homopropargylic alcohols. Thus, *tert*-homopropargylic alcohol was added dropwise to a mixture of a palladium catalyst and $(i\mathrm{Pr}_2\mathrm{N})_2\mathrm{BCN}$ (1.2 equiv.) under reflux in toluene (Eq. (8)). This one-pot procedure afforded the corresponding product **4a** in a 94% yield. Although this procedure was not applicable to the cyanoboryl ethers derived via Route A, the one-pot procedure demonstrated the synthetic flexibility of intramolecular cyanoboration reactions.



(8)

We propose the following reaction mechanism for intramolecular cyanoboration (Scheme 3). Initially, the alkyne moiety of **1** coordinates to palladium (to form **A**). The B–CN bond is then activated by the palladium center, leading to the formation of a (boryl) (cyano)palladium(II) intermediate **B**. The intermediate **B** may undergo facile insertion of the carbon–carbon triple bond into its B–Pd bond, giving the (alkenyl)(cyano)palladium(II)

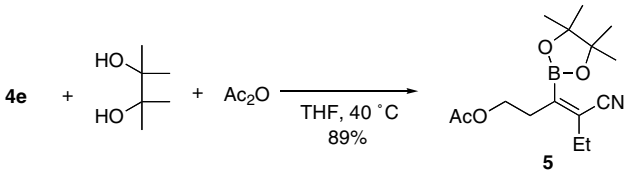


Scheme 3. A possible reaction mechanism of the intramolecular cyanoboration.

intermediate **C**. Reductive elimination of a carbon–carbon bond then affords the cyanoboration product **4**.

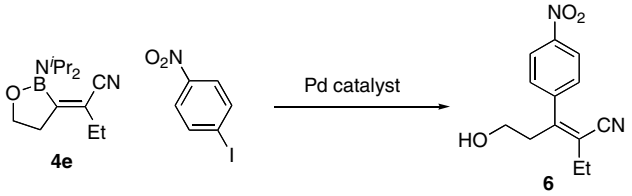
4. Synthetic application of cyanoboration products

The product **4** obtained in the intramolecular cyanoboration reactions is a convenient synthetic intermediate for obtaining α,β-unsaturated nitriles having a defined stereochemistry. Although these are chromatographically unstable, treatment of the 5-membered cyclic boryl ether **4e** with pinacol and acetic anhydride at 40 °C afforded a pinacolborane derivative **5** with an acetoxy group (Eq. (9)). The pinacol derivative **5** was found to be stable toward silica gel chromatography.



(9)

Particular attention was paid to C–C bond forming reactions at the boryl group for the synthesis of highly substituted α,β-unsaturated nitriles. As an initial attempt, a Suzuki–Miyaura coupling [12] was applied to the intramolecular cyanation product **4e**. *p*-Nitroiodobenzene reacted with **4e** in the presence of a palladium/tri-*tert*-butylphosphine catalyst with KF [13], giving the fully substituted α,β-unsaturated nitrile **6** (Eq. (10)). It should be noted that no desired product was formed using catalytic quantities of a tetrakis(triphenylphosphine)palladium complex with sodium ethoxide as a base. Under the same reaction conditions using *t*-Bu_3P, the Suzuki–Miyaura coupling of **4e** with iodobenzene and *p*-iodotoluene was also achieved, giving **7** and **8**, respectively, in high yields (Eq. (11)).



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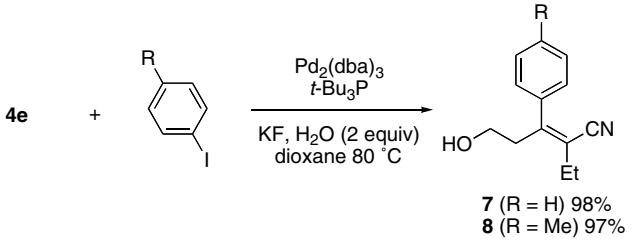
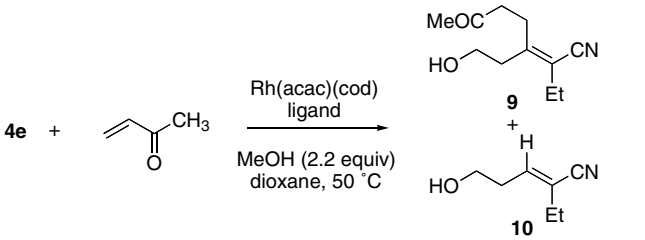


(11)

We then examined the rhodium-catalyzed conjugative addition of organoborane reagents to enones. According to an original report by Miyaura [14], we initially used 1,4-bis(diphenylphosphino)butane (dppb) as the ligand on rhodium. In the reaction of **4e** with methyl vinyl ketone (MVK), however, the dppb-Rh system gave significant amounts of the protodeborylation by-product **10** along with the desired conjugative addition product **9**. Even in the best case, where MeOH was used as an additive, the conjugative addition product **9** was obtained in only a 68% yield, along with **10** in a ratio of 82:18 (Eq. (12)). This difficulty was finally overcome by using bidentate phosphine ligands that carry shorter

tethers connecting the two phosphine atoms. In the presence of bis(diphenylphosphino)propane (dppp) or bis(diphenylphosphino)ethane (dppe) ligands on rhodium, **9** was obtained selectively in a high yield with no formation of **10**. These results also suggested to us that the dppb-Rh catalyst system was good for protodeborylation in the absence of MVK, and **4e** afforded **10** selectively in a 96% yield in the presence of a Rh-dppb catalyst at 80 °C in wet dioxane (Eq. (13)).



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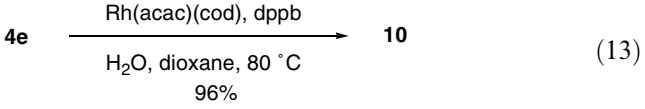

(13)

5. Conclusion

The B–CN bond of cyanoborane is activated by palladium and nickel complexes, leading to an intramolecular *cis*-addition to a carbon–carbon triple bond in a 5-exo fashion. This is the first clear demonstration of the activation of a B–CN bond by transition-metal catalysts. From the synthetic point of view, this reaction offers novel accesses to highly substituted α,β-unsaturated nitriles via C–C or C–H bond forming reactions at the boryl group, such as palladium-catalyzed Suzuki–Miyaura coupling and rhodium-catalyzed Miyaura conjugate addition. Although cyanoboranes have not been utilized in synthetic organic chemistry since their appearance in the late 1950s, this, and some recent findings, on the reactivity of this "forgotten" reagent may help increase intensive studies on their unique functions in organic synthesis. Related projects focusing on B–CN bond activation are now being undertaken in this laboratory [15].

6. Experimental

6.1. General

All reactions were performed under a nitrogen atmosphere with magnetic stirring. Column chromatography was performed with Wakogel C-200 (silica gel, 75–150 μm, Wako). ^{1}H and ^{13}C NMR spectra were recorded on a Mercury vx400 spectrometer at ambient temperature.

Anhydrous THF (Kanto) and dioxane (Wako) were purchased from the commercial sources. Toluene was distilled from $LiAlH_4$ under nitrogen. $Pd(acac)_2$ (Mitsuwa), $PdCl_2$ (Furuya Kinzoku, Co.), $Ni(COD)_2$ (Aldrich), Rh(acac)(COD) (Aldrich), iodobenzene (Wako), *p*-iodonitrobenzene (TCI), *p*-iodotoluene (TCI), pinacol (TCI), acetic anhydride (Wako), tri(*t*-butyl)phosphine (Aldrich), KF (spray dried, Wako), and 1,4-bis(diphenylphosphino)butane (dppb, Kanto) were used as received from the commercial sources. Methyl vinyl ketone (Wako) was obtained from the commercial source and purified by distillation. $Pd(PPh_3)_4$ [16], $Pd_2(dba)_3$-benzene [17], $PdCl_2(MeCN)_2$ [18], bis(diisopropylamino)cyanoborane [8], and 4-methyl-1-heptyn-4-ol [19] were prepared according to the literature methods.

6.2. Preparation of (diisopropylamino)cyanoboryl homopropargyl ethers *1*

6.2.1. Representative procedure for the preparation of *1h* from secondary homopropargyl alcohols (Route A1)

To a solution of dichloro(diisopropylamino)borane (1.82 g, 10.0 mmol) in hexane (10 mL) and CH_2Cl_2 (5 mL) were added triethylamine (1.67 mL, 12.0 mmol) and 5-hexyn-3-ol (941 mg, 9.5 mmol) at −78 °C. The reaction mixture was stirred for 4 h, while the reaction temperature was gradually raised to room temperature. The mixture was further stirred at room temperature for 10 h. To this mixture was added trimethylsilylcyanide (1.60 mL, 12 mmol) at room temperature, and the resultant mixture was stirred for 1 h at room temperature. After evaporation of the solvent was added hexane to the residue. The insoluble precipitates were filtered off and washed with hexane twice. Evaporation of the solvent followed by bulb-to-bulb distillation (100 °C/2 mmHg) yielded **1h** (1.97 g, 84%).

6.2.2. Representative procedure for the preparation of *1g* from primary homopropargyl alcohols (Route A2: 3 steps)

Step 1: A mixture of boric acid (415 mg, 6.71 mmol) and 6-methyl-5-hepten-3-yn-1-ol (3.0 g, 24.2 mmol) in toluene (15 mL) was stirred under reflux for 12 h with removal of water by a Dean-Stark trap. Evaporation of the solvent followed by bulb-to-bulb distillation (180–230 °C/0.5 mmHg) yielded **3g** (2.90 g, 99% based on boric acid). *Step 2*: A mixture of **3g** (2.9 g, 7.62 mmol), boron trichloride dimethylsulfide complex (737 mg, 4.11 mmol), and chlorobis(diisopropylamino)borane (2.89 g, 11.7 mmol) was heated in toluene (3 mL) with stirring at 80 °C for 16 h. Bulb-to-bulb distillation (120–150 °C/1 mmHg) yielded **2g** (5.21 g, 85%). *Step 3*: A mixture of **2g** (5.0 g, 18.5 mmol) and

trimethylsilyl cyanide (2.72 mL, 20.4 mmol) was stirred at room temperature for 5 h. Bulb-to-bulb distillation (120–160 °C/1 mmHg) yielded **1g** (4.70 g, 97%).

6.2.3. Representative procedure for the preparation of *1a* from tertiary homopropargyl alcohols (Route B)

To a solution of bis(diisopropylamino)cyanoborane (474 mg, 2.0 mmol) in THF (1 mL) was added 4-methyl-1-heptyn-4-ol (265 mg, 2.1 mmol) at room temperature. The mixture was heated at 40 °C for 20 h. Evaporation of the solvent followed by bulb-to-bulb distillation (120–150 °C/1.0 mmHg) afforded **3a** (445 mg, 85%) as colorless oil. **3a**: ^{1}H NMR (C_6D_6) δ 0.82 (t, J = 7.2 Hz, 3H), 0.88 (d, J = 6.6 Hz, 6H), 1.13 (dd, J = 6.6, 2.4 Hz, 6H), 1.17–1.32 (m, 2H), 1.43 (s, 3H), 1.71–1.87 (m, 3H), 2.41 (dd, J = 16.8, 2.4 Hz, 1H), 2.50 (dd, J = 16.8, 2.4 Hz, 1H), 3.02 (sep, J = 6.6 Hz, 1H), 4.01 (sep, J = 6.6 Hz, 1H); ^{13}C NMR (C_6D_6) δ 14.7, 17.7, 22.3, 23.1, 26.2, 31.8, 42.9, 45.0, 49.8, 71.5, 78.7, 81.1; ^{11}B NMR (C_6D_6) δ 16.9; IR (neat) 2215 cm^{-1}. Anal. Calc. for $C_{15}H_{27}BN_2O$: C, 68.71; H, 10.38; N, 10.68. Found: C, 68.63; H, 10.19; N, 10.43%.

6.3. Intramolecular cyanoboration

6.3.1. General procedure for the optimization of the reaction conditions (Table 1)

A mixture of a catalyst (0.015 mmol Pd or Ni), **1a** (79 mg, 0.30 mmol), and *m*-dimethoxybenzene (internal standard, 20.0 μL, 21.1 mg) in toluene-d_8 (0.50 mL) was stirred at 50 °C. After 3 h, the reaction mixture was cooled to room temperature and was subjected to a ^{1}H NMR measurement. In cases where cyanoboration was taking place, the mixture was heated further at 50 °C. When no reaction was observed by the NMR measurement, the mixture was heated to 80 °C for 3 h, and the progress of the reaction was then checked by an NMR measurement. Finally, the temperature was raised to 110 °C (bath temp.) to observe the progress of the cyclization, if no reaction took place at 80 °C. Final reaction yield was determined from the integrations of ^{1}H NMR spectrum of the reaction mixture.

6.3.2. Representative procedure for the cyanoboration of *1e* in a preparative scale

A mixture of $Pd(PPh_3)_4$ (578 mg, 0.50 mmol) and **1e** (2.34 g, 10.0 mmol) in toluene (17 mL) was heated at 120 °C for 43 h with stirring. Evaporation of the solvent followed by bulb-to-bulb distillation (120 °C/1.0 mmHg) afforded **4e** (2.20 g, 94%).

6.3.3. Procedure for the one-pot reaction of homopropargylic alcohol with bis(diisopropylamino)-cyanoborane

To a mixture of $Pd_2(dba)_3$benzene (15 mg, 0.015 mmol) and bis(diisopropylamino)cyanoborane (171 mg, 0.72 mmol) in toluene (1.0 mL) was added the 3-methylhept-6-yn-3-ol (76 mg, 0.60 mmol) dropwise over 1 min at 120 °C (bath temperature). The mixture was further stirred for 3 h at 120 °C. After the mixture was cooled to room temperature, the solvent was evaporated. To the residue, benzene-d_6 (ca. 1 mL) and 2,6-dimethylanisol (internal standard, 19.5 mg, 0.14 mmol) were added. The reaction yield of **4a** (94%) was determined by a ^{1}H NMR measurement.

(*E*)-*2-Diisopropylamino-5-methyl-5-propyl-3-cyanomethylene-1,2-oxaborolane* (***4a***). ^{1}H NMR (C_6D_6) δ 0.77 (t, J = 6.8 Hz, 3H), 0.91 (s, 3H), 1.03–1.44 (m, 16H), 1.83 (d, J = 14.8 Hz, 1H), 2.02 (d, J = 14.8 Hz, 1H), 2.85–3.20 (br, 1H), 4.12–4.44 (br, 1H), 5.12 (s, 1H); ^{13}C NMR (C_6D_6) δ 14.9, 18.1, 23.4, 27.0, 44.8, 45.1, 50.4, 51.6, 80.8, 102.4, 117.9, 167.0; ^{11}B NMR (C_6D_6) δ 27.9; IR (neat) 2215 cm^{-1}. Anal. Calc. for $C_{15}H_{27}BN_2O$: C, 68.71; H, 10.38; N, 10.68. Found: C, 68.56; H, 10.45; N, 10.67%.

(*E*)-*2-Diisopropylamino-3-cyanomethylene-1-oxa-2-boraspiro[4.5]decane* (***4b***). ^{1}H NMR (C_6D_6) δ 1.00–1.50 (m, 20H), 1.54–1.70 (m, 2H), 1.94 (d, J = 2.8 Hz, 2H), 2.80–3.38 (br, 1H), 4.00–4.57 (br, 1H), 5.15 (s, 1H); ^{13}C NMR (C_6D_6) δ 23.4, 26.0, 38.6, 45.0, 50.5, 52.1, 80.1, 102.5, 117.9, 166.1; ^{11}B NMR (C_6D_6) δ 27.7; IR (neat) 2211 cm^{-1}. Anal. Calc. for $C_{16}H_{27}BN_2O$: C, 70.08; H, 9.92; N, 10.22. Found: C, 69.80; H, 9.66; N, 10.03%.

(*E*)-*2-Diisopropylamino-3-(1-cyanopropylidene)-1-oxa-2-boraspiro[4.5]decane* (***4c***). ^{1}H NMR (C_6D_6) δ 0.91 (t, J = 7.5 Hz, 3H), 0.99–1.16 (m, 3H), 1.22–1.52 (m, 17H), 1.57–1.73 (m, 2H), 1.90 (q, J = 7.5 Hz, 2H), 1.94 (s, 2H), 3.20–4.22 (br, 2H); ^{13}C NMR (C_6D_6) δ 12.9, 23.4, 26.2, 27.8, 38.8, 46.8, 47.4, 79.9, 119.3, 120.0, 157.1; ^{11}B NMR (C_6D_6) δ 27.7; IR (neat) 2207 cm^{-1}. Anal. Calc. for $C_{18}H_{31}BN_2O$: C, 71.52; H, 10.34; N, 9.27. Found: C, 71.40; H, 10.41; N, 9.12%.

(*E*)-*2-Diisopropylamino-3-cyanobenzylidene-5,5-dimethyl-1,2-oxaborolane* (***4d***). M.p. 87.0–87.9 °C: ^{1}H NMR (C_6D_6) δ 0.90 (s, 6H), 1.33 (d, 12H), 2.27 (s, 2H), 6.92–7.05 (m, 3H), 7.20–7.26 (m, 2H); ^{13}C NMR (C_6D_6) δ 23.4, 29.3, 48.1, 50.4, 79.0, 119.0, 119.9, 129.05, 129.10, 129.5, 137.1, 160.3; ^{11}B NMR (C_6D_6) δ 29.1; IR (neat) 2207 cm^{-1}. Anal. Calc. for $C_{19}H_{27}BN_2O$: C, 73.56; H, 8.77; N, 9.03. Found: C, 73.72; H, 8.65; N, 8.95%.

(*E*)-*2-Diisopropylamino-3-(1-cyanopropylidene)-1,2-oxaborolane* (***4e***). ^{1}H NMR (C_6D_6) δ 0.87 (t, J = 7.5 Hz, 3H), 1.25 (d, J = 6.6 Hz, 12H), 1.88 (q, J = 7.5 Hz, 2H), 1.98 (t, J = 6.6 Hz, 2H), 3.57 (t, J = 6.6 Hz, 2H), 3.44–3.89 (br, 2H); ^{13}C NMR (C_6D_6) δ 12.9, 23.4, 27.9, 35.2, 47.7, 66.2, 119.2, 119.8, 156.4; ^{11}B NMR (C_6D_6) δ 29.1; IR (neat) 2209 cm^{-1}. Anal. Calc. For $C_{13}H_{23}BN_2O$: C, 66.68; H, 9.90; N, 11.96. Found: C, 66.95; H, 9.78; N, 11.74%.

(*E*)-*2-Diisopropylamino-3-(1-cyanoethylidene)-5-ethyl-1,2-oxaborolane* (***4f***). ^{1}H NMR (C_6D_6) δ 0.80

(t, J = 7.2 Hz, 3H), 1.12–1.40 (m, 14H), 1.48 (s, 3H), 1.66 (dd, J = 15.2, 6.8 Hz, 1H), 2.08 (dd, J = 15.2, 6.0 Hz, 1H), 3.64 (quint, J = 6.0 Hz, 1H); ^{13}C NMR (C_6D_6) δ 10.2, 20.5, 23.4, 30.9, 41.0, 78.2, 111.8, 120.8, 157.4; ^{11}B NMR (C_6D_6) δ 28.7; IR (neat) 2209 cm^{-1}. Anal. Calc. for $C_{14}H_{25}BN_2O$: C, 67.76; H, 10.15; N, 11.29. Found: C, 67.62; H, 10.19; N, 11.33%.

(*E*)-*2-(2-Diisopropylamino-[1,2]oxaborolan-3-ylidene)-4-methylpent-3- enenitrile* (***4g***). ^{1}H NMR (C_6D_6) δ 1.29 (d, J = 6.9 Hz, 12H), 1.44 (d, J = 1.5 Hz, 3H), 1.51 (d, J = 1.5 Hz, 3H), 2.05 (dt, J = 6.6, 0.6 Hz, 2H), 3.49–3.95 (br, 2H), 3.59 (t, J = 6.6 Hz, 2H), 5.47–5.51 (m, 1H);^{13}C NMR (C_6D_6) δ 19.9, 23.4, 26.2, 37.0, 47.8, 66.3, 114.6, 119.5, 121.4, 140.9, 157.6; ^{11}B NMR (C_6D_6) δ 29.1; IR (neat) 2211 cm^{-1}. Anal. Calc. for $C_{16}H_{27}BN_2O$: C, 69.24; H, 9.68; N, 10.77. Found: C, 69.12; H, 9.80; N, 10.73%.

(*E*)-*2-Diisopropylamino-3-cyanomethylene-5-ethyl-1,2-oxaborolane* (***4h***). ^{1}H NMR (C_6D_6) δ 0.75 (t, J = 7.2 Hz, 3H), 1.00–1.45 (m, 14H), 1.73 (dd, J = 14.8, 6.8 Hz, 1H), 1.94 (dd, J = 14.8, 6.0 Hz, 1H), 2.88–3.14 (br, 1H), 4.14–4.46 (br, 1H), 3.59 (quint, J = 6.8 Hz, 1H); ^{13}C NMR (C_6D_6) δ 10.1, 23.3, 30.5, 44.5, 45.9, 50.5, 78.4, 102.1, 117.9, 165.8; ^{11}B NMR (C_6D_6) δ 28.1; IR (neat) 2216 cm^{-1}. Anal. Calc. for $C_{13}H_{23}BN_2O$: C, 66.68; H, 9.90; N, 11.96. Found: C, 66.82; H, 10.12; N, 12.03%.

(*E*)-*2-Diisopropylamino-3-cyanomethylene-1,2-oxaborolane* (***4i***). ^{1}H NMR (C_6D_6) δ 1.26 (d, J = 5.4 Hz, 12H), 1.91 (dt, J = 2.1, 6.3 Hz, 2H), 2.80–4.50 (br, 2H), 3.53 (t, J = 6.3 Hz, 2H), 5.09 (s, 1H); ^{13}C NMR (C_6D_6) δ 23.3, 23.4, 40.6, 51.2, 66.1, 102.3, 117.8, 165.1; ^{11}B NMR (C_6D_6) δ 28.3; IR (neat) 2215 cm^{-1}. Anal. Calc. for $C_{11}H_{19}BN_2O$: C, 64.11; H, 9.29; N, 13.59. Found: C, 64.23; H, 9.11; N, 13.73%.

6.4. Reactions of cyanoboration products

6.4.1. Synthesis of acetic acid (E)-4-cyano-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)hex-3-enyl ester (5)

To a mixture of **4e** (70 mg, 0.30 mmol) and pinacol (43 mg, 0.36 mmol) in THF (1 mL) was added acetic anhydride (34 μL, 0.36 mmol) at room temperature. The mixture was heated with stirring at 40 °C for 11 h. Evaporation followed by bulb-to-bulb distillation (230–280 °C/1 mmHg) yielded **5** (78 mg, 89%). **5**: ^{1}H NMR ($CDCl_3$) δ 1.16 (t, J = 7.6 Hz, 3H), 1.31 (s, 12H), 2.02 (s, 3H), 2.35 (q, J = 7.6 Hz, 2H), 2.61 (t, J = 6.8 Hz, 2H), 4.10 (t, J = 6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 12.5, 20.8, 24;.4, 24.6, 29.9, 62.6, 84.7, 118.6, 128.1, 171.0; ^{11}B NMR (C_6D_6) δ 29.1; IR (neat) 2215, 1740 cm^{-1}. HRFABMS Calc. for $C_{15}H_{25}BNO_4$ (M+H$^+$): 294.1877. Found: 294.1878.

6.4.2. Synthesis of (Z)-2-ethyl-5-hydroxy-3-p-nitrophenylpent-2-enenitrile (6)

To a mixture of $Pd_2(dba)_3 \cdot$ benzene (6.0 mg, 0.006 mmol), tri-*t*-butylphosphine (3.6 μL, 0.0144 mmol), potassium fluoride (58 mg, 0.99 mmol), water (11 mg, 0.60 mmol) and *p*-iodonitrobenzene (90 mg, 0.36 mmol) in dioxane (1.0 mL) was added **4e** (70 mg, 0.30 mmol) at room temperature. The mixture was heated with stirring at 80 °C for 4 h. Water is added to the reaction mixture, and organic material was extracted with ethyl acetate three times. Evaporation followed by preparative TLC (hexane: ethyl acetate = 2:1) yielded **6** (71 mg, 96%). **6**: m.p. 77.3–77.6 °C: ^{1}H NMR ($CDCl_3$) δ 1.24 (t, J = 7.5 Hz, 3H), 1.72 (br, 1H), 2.47 (q, J = 7.5 Hz, 2H), 2.81 (t, J = 6.3 Hz, 2H), 3.57 (t, J = 6.3 Hz, 2H), 7.51 (d, J = 9.0 Hz, 2H), 8.24 (d, J = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 12.8, 24.1, 36.2, 59.6, 117.3, 118.2, 123.9, 129.1, 146.4, 147.8, 152.6; IR (neat) 3261, 2211 cm^{-1}. HRMS Calc. for $C_{13}H_{14}N_2O_3$ (M$^+$): 264.1004. Found: 264.1004.

6.4.3. Synthesis of (Z)-2-ethyl-5-hydroxy-3-phenylpent-2-enenitrile (7)

By a similar procedure to that of **6**, the title compound **7** was prepared from **4e** (1.55 g, 6.62 mmol) and iodobenzene (1.45 g, 7.1 mmol). 0.5 mol% of $Pd_2(dba)_3$ complex with *t*-Bu_3P and KF was used. Yield 1.31 g, 98%. **7**: ^{1}H NMR ($CDCl_3$) δ 1.23 (t, J = 7.6 Hz, 3H), 1.97 (s, 1H), 2.43 (q, J = 7.6 Hz, 2H), 2.77 (t, J = 6.4 Hz, 2H), 3.51 (t, J = 6.4 Hz, 2H), 7.27–7.40 (m, 5H);^{13}C NMR ($CDCl_3$) δ 13.2, 24.2, 36.8, 59.9, 114.9, 118.9, 127.5, 128.3, 128.6, 139.3, 154.3. HRMS Calc. for $C_{13}H_{15}NO$ (M$^+$): 201.1154. Found: 201.1158.

6.4.4. Synthesis of (Z)-2-ethyl-5-hydroxy-3-p-tolylpent-2-enenitrile (8)

By a similar procedure to that of **6**, the title compound **8** was prepared from **4e** (70 mg, 0.30 mmol) and *p*-iodotoluene (79 mg, 0.36 mmol). The reaction was conducted for 10 h, and a mixture of hexane/ethyl acetate (3:1) was used as eluent for preparative TLC. The product yield was 97% (63 mg). **8**: ^{1}H NMR ($CDCl_3$) δ 1.22 (t, J = 7.6 Hz, 3H), 1.75 (s, 1H), 2.36 (s, 3H), 2.43 (q, J = 7.6 Hz, 2H), 2.78 (t, J = 6.8 Hz, 2H), 3.53 (t, J = 6.8 Hz, 2H);^{13}C NMR ($CDCl_3$) δ 13.0, 21.1, 24.1, 36.6, 60.0, 114.6, 119.3, 127.7, 129.3, 136.6, 138.9, 154.5; IR (neat) 3430, 2211 cm^{-1}. HRMS Calc. for $C_{14}H_{17}NO$ (M$^+$): 215.1310. Found: 215.1310.

6.4.5. Synthesis of (E)-2-ethyl-3-(2-hydroxyethyl)-6-oxohept-2-enenitrile (9)

To a mixture of Rh(acac)(cod) (2.8 mg, 0.009 mmol), dppb (3.8 mg, 0.009 mmol), **4e** (70 mg, 0.30 mmol), methyl vinyl ketone (50 μL, 0.60 mmol), and methanol (27 μL, 0.66 mmol) in dioxane (1.0 mL) was heated at 50 °C for 22 h. To the was added water mixture cooled

to room temperature, and organic material was extracted with AcOEt. Evaporation followed by column chromatography on silica gel (hexane:AcOEt = 2/1–1/2) afforded **9** (40 mg, 68%). ^{1}H NMR ($CDCl_3$) δ 1.11 (t, J = 7.5 Hz, 3H), 2.17 (s, 3H), 2.25 (q, J = 7.5 Hz, 2H), 2.43 (t, J = 6.6 Hz, 2H), 2.64 (s, 4H), 3.70 (t, J = 6.6 Hz, 2H);^{13}C NMR ($CDCl_3$) δ 12.9, 23.1, 29.6, 29.7, 30.0, 34.7, 41.6, 60.3, 114.7, 118.5, 154.2; IR (neat) 3348, 2209, 1717 cm^{-1}. HRCIMS Calc. for $C_{11}H_{17}NO_2$ (M^+):195.1259. Found: 195.1260.

*6.4.6. Synthesis of (E)-2-ethyl-5-hydroxypent-2-enenitrile (**10**)*

To a mixture of Rh(acac)(cod) (2.8 mg, 0.009 mmol) and 1,4-bis(diphenylphosphino)butane (3.8 mg, 0.009 mmol) in dioxane (1 mL) were added **4e** (70 mg, 0.03 mmol) and water (21.6 μL, 1.2 mmol) at room temperature. The mixture was stirred at 50 °C for 20 h. Water is added to the reaction mixture at room temperature and the organic material was extracted with ethyl acetate. Column chromatography on silica gel afforded **10** (36 mg, 96%). **10**: ^{1}H NMR ($CDCl_3$) δ 1.12 (t, J = 7.5 Hz, 3H), 2.10–2.29 (br, 1H), 2.24 (q, J = 7.5 Hz, 2H), 2.42 (q, J = 6.6 Hz, 2H), 3.67 (t, J = 6.6 Hz, 2H), 6.36, (t, J = 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 12.5, 22.0, 31.5, 60.7, 118.3, 119.6, 143.8; IR (neat) 3411, 2217 cm^{-1}. HRCIMS Calc. for $C_7H_{12}NO$ (M+H$^+$): 126.0919. Found: 126.0919.

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