Dienophilic Activity of Vinyldichloroboranes and their Use as Partners in Diels–Alder—Reductive Alkylation of Azides in a One-pot Reaction

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Vinyldichloroboranes react with 1,3-dienes and the sequence Diels–Alder cycloaddition–reductive alkylation of benzyl azide leads directly to secondary amines, therefore, showing that vinyldichloroboranes behave as synthetic equivalents of secondary enamines of defined stereochemistry.

Vinylboronic esters are not very reactive towards 1,3-dienes and high temperatures are required in order to obtain the Diels–Alder adducts, the reported examples of such cycloadditions are, therefore, scarce[1] although the very broad synthetic potential of the carbon–boron bond[2] makes this approach to new boranes very attractive. One way to increase the reactivity of the double bond of vinylboronates, *i.e.* the replacement of one of the vinylic hydrogens β to the boryl group by an electron-withdrawing group was recently described.[3] Such electron poor alkenes react with cyclopentadiene at temperatures as low as −10 °C.[4] A high reactivity of 9-vinyl-9-borabicyclo[3.2.1]nonane (vinyl-9-BBN) and 2-trimethylsilylvinyl-9-BBN as dienophiles was recently reported by Singleton *et al.*[5,6]

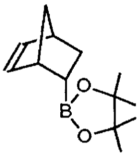
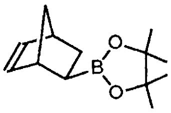
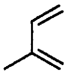
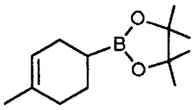
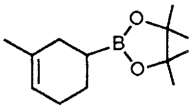
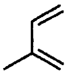
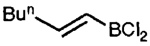
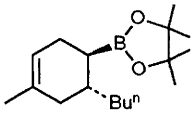
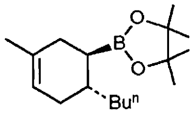
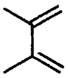
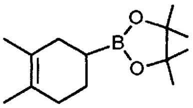
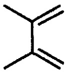
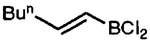
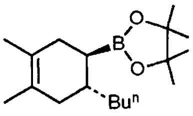
Owing to the interest in dichloroboranes for the creation of C–N[7] or C–C[8] bonds and our interest in this chemistry[9] we initiated a study of the reactivity of dihalovinylboranes towards 1,3-dienes and report here our first results in this area.

The reactions of vinyldichloroboranes with some simple dienes[10] are summarized in Table 1. The adducts were not isolated as the dichloro derivatives but as the boronic esters derived from pinacol obtained by addition of one equivalent of pinacol to the crude reaction mixture.

It can be seen from Table 1 that vinyldichloroborane is a reactive dienophile leading to Diels–Alder adducts with simple dienes such as cyclopentadiene, isoprene and 2,3-dimethylbuta-1,3-diene in good to excellent yields. It may be worth noting that these results could only be obtained in toluene as solvent and when reagents were mixed at low temperature. The same reactions carried out in dichloromethane or hexane did not give exploitable results. The reaction with cyclopentadiene gave a 1 : 1 mixture of *endo* and *exo* adducts while that with isoprene gave a 3 : 2 mixture of the 1,4- and 1,3-disubstituted adducts. These results are close to those observed with dibutyl vinylboronate.[1]

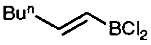
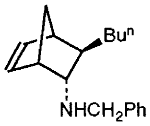
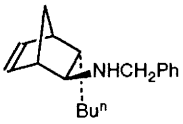
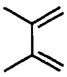
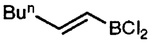
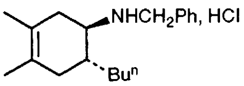
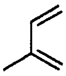
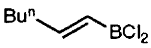
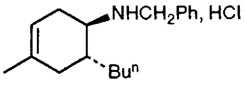
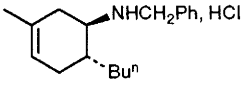
We then studied the reactivity of the disubstituted alkene (1*E*)-hex-1-en-1-yldichloroborane prepared either by reaction

Table 1 Products and yields for Diels–Alder reactions with vinyldichloroboranes

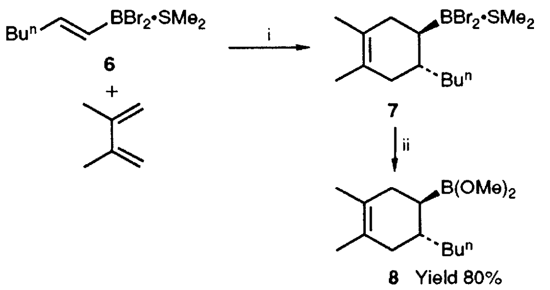
Diene	Alkene	Isolated yield (%)	Products and ratio
		60[a]	 +  1 : 1 **1** **1′**
		86[a]	 +  3 : 2 **2** **2′**
		47[b]	 +  7 : 3 **3** **3′**
		85[a]	 **4**
		54[b]	 **5**

[a] General procedure: Purified vinyldichloroborane[11] was added to 1.5–2 equiv. of diene in anhydrous toluene at −78 °C under argon and the reaction mixture allowed to warm slowly over 12 h. Then, one equivalent of pinacol was added and the adducts purified by Kügelrohr distillation. [b] General procedure: (1*E*)-hex-1-en-1-yldichloroborane was added to 1.5–2 equiv. of diene in anhydrous toluene at room temperature under argon. The reaction mixture was heated for 3 h at 110 °C in a sealed tube. After cooling, aqueous sodium hydroxide was added followed by addition of 1 equiv. of pinacol and diethyl ether extraction. Products were purified by column chromatography on silica gel followed by bulb-to-bulb distillation.

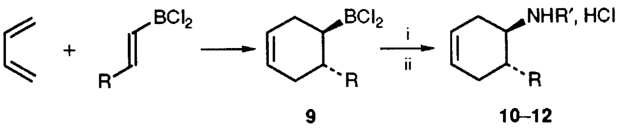
Table 2 Products and yields for tandem Diels–Alder—reductive alkylation of benzyl azide

Diene	Alkene	Isolated yield (%)	Products and ratio
		45[a]	 +  **10** **10′**
		72[b]	 **11**
		85	 +  7 : 3 **12** **12′**

[a] Isolated as the free amine by bulb-to-bulb distillation as a 55 : 45 mixture of *endo* and *exo* isomers after column chromatography of the crude reaction mixture (diethyl ether–heptane, 20 : 80, $R_f = 0.3$). [b] See text.



Scheme 1 *Reagents and conditions*: i, heat, benzene; ii, MeOH



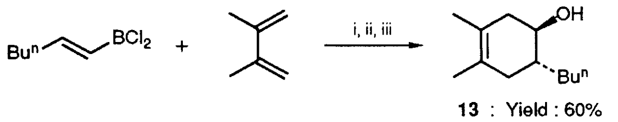
Scheme 2 *Reagents*: i, $R'N_3$; ii, MeOH

of the corresponding boronic acid[12] with an excess of trichloroborane in refluxing hexane for 2 h followed by distillation (b.p. 58–59 °C/15 mmHg, 68% yield)[13] or by using the very efficient method of Matteson[14] for the *in situ* generation of $HBCl_2$ at low temperature in the presence of hex-1-yne (87% yield). The reaction of this disubstituted alkene with an excess of diene was carried out in toluene at 110 °C for 3 h. Longer reaction times at lower temperatures did not give satisfactory results. After hydrolysis and esterification with pinacol, the boronic esters **3** + **3′** and **5** were purified by column chromatography followed by Kügelrohr distillation. A 7 : 3 mixture of the regioisomers **3** and **3′** was obtained with isoprene, in favour of the 1,4-isomer **3**. The (1*E*)-hex-1-en-1-yldibromoborane dimethyl sulfide **6** easily prepared by hydroboration of hex-1-yne with $HBBr_2{\cdot}SMe_2$ at room temperature[15] reacted with 2,3-dimethylbuta-1,3-diene in refluxing benzene for 3 h to give, after methanolysis, the boronate **8** isolated in 80% yield after bulb-to-bulb distillation (Scheme 1). Thus, the alkene **6** shows good reactivity as a dienophile.

The practicability of the reaction being secured, we envisioned using the vinyldichloroboranes as synthetic equivalents of secondary enamines according to Scheme 2.

The dichloroboranes **9** obtained *via* a Diels–Alder cycloaddition should react with azides to give after methanolysis the hydrochlorides **10–12**.[7,9] One major interest of this reductive alkylation of azides is in the replacement of the carbon–boron bond by a carbon–nitrogen bond with retention of configuration.[7] Our first results along this line are reported in Table 2.

The preparation of **11**† is representative of this one-pot sequence: freshly distilled 2,3-dimethylbuta-1,3-diene (3.39 ml, 30 mmol) was added to a 20 ml solution of 10 mmol of (1*E*)-hex-1-en-1-yldichloroborane (1.65 g) under nitrogen. The reaction mixture was then heated for 3 h at 110 °C (oil bath temperature). After cooling, 1.33 g of benzyl azide (10 mmol) was slowly added *via* a syringe. Nitrogen evolution soon started. After 4 h at room temperature, methanol (2 ml) was added, the reaction mixture stirred for an additional hour and then the volatiles removed under vacuum. Washing the crude product with diethyl ether and recrystallisation from acetonitrile gave 2.22 g of pure **11**. It can be seen from Table 2 that this one-pot, two-step sequence, gives the secondary amines in good yields and clearly shows the interest of vinyldichloroboranes as synthetic equivalents of secondary enamines.



Scheme 3 *Reagents and conditions*: i, toluene, 3 h, 110 °C; ii, $NaOH–H_2O_2$, −15 °C → room temp.; iii, purification by bulb-to-bulb distillation

Vinyldichloroboranes could also be used as synthetic equivalents of enols of defined stereochemistry. This is illustrated by the example shown in Scheme 3.

Thus, the reaction of (1*E*)-hex-1-en-1-yldichloroborane with 2,3-dimethylbuta-1,3-diene in toluene at 110 °C for 3 h followed by an oxidation by hydrogen peroxide in basic medium at low temperature gave the cyclohexenol **13**‡ isolated in a 60% yield.

The use of such strategies for the construction of heterocyclic systems is under active investigation.

Received, 8th May 1992; Com. 2/02377F

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† **11**: Yield 72%, m.p. 166–167 °C. ^1H NMR (300 MHz) $CDCl_3$ + D_2O, δ: 0.83 (t, 3H, *J* 7.3 Hz); 1.0–1.4 (m, 4H); 1.55 (s, 6H); 1.6–1.8 (m, 1H); 2.0–2.5 (m, 4H); 2.90 (ddd, 1H, *J* 5.7, 5.8 and 6.7 Hz); 4.15 (d, 1H, *J* 14.8 Hz); 4.34 (d, 1H, *J* 14.8 Hz); 7.2–7.4 (m, 3H); 7.7–7.8 (m, 2H). ^{13}C NMR (75.5 MHz) $CDCl_3$ + D_2O, δ: 14.1; 18.8; 18.9; 22.6; 28.3; 31.4; 31.5; 34.0; 34.1; 47.7; 54.3; 120.5; 125.2; 129.1; 129.2; 130.3; 130.6.

‡ **13**. Yield 60%, b.p.$_{0.05}$ = 65–70 °C. ^1H NMR (300 MHz) $CDCl_3$; δ: 0.91 (t, 3H, *J* 7.4 Hz); 1.02–1.50 (m, 5H); 1.58–1.73 (m, 3H); 1.60 (s, 6H); 1.91–2.30 (m, 4H); 3.57 (ddd, 1 H *J* 5.3, 8.1 and 8.3 Hz). ^{13}C NMR (75.5 MHz) $CDCl_3$, δ: 14.1; 18.6; 18.8; 23.1; 29.0; 31.5; 36.2; 40.2; 40.7; 122.7; 124.8.