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LETTERS

B-(2-Azido-2-propenyl)-1,3,2-dioxaborinane: A Novel Reagent for Allylboration

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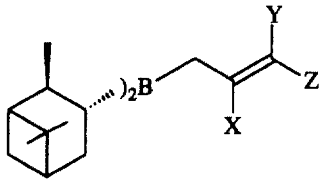
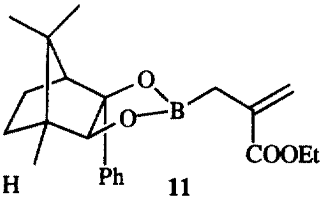
Abstract: A new allylborating agent, *B*-(2-azido-2-propenyl)-1,3,2-dioxaborinane, has been synthesized by the reaction of iodine azide with B-allyl-1,3,2-dioxaborinane, followed by dehydroiodination with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). This reagent allylborates representative aldehydes to provide, after hydrogen peroxide oxidation, the corresponding 2-azido-1-alken-4-ols in 64-75% isolated yields.

Allylboration and related reactions of aldehydes, ketones and imines are well established procedures for acyclic stereoselection.[2] During the past 15 years we have developed several versatile reagents for enantioselective and diastereoselective synthesis of homoallylic alcohols.[3] Many of these reagents have found wide application in organic synthesis. These include, *B*-allyldiisopinocampheylborane (1),[4] [*Z*]- and [*E*]-crotyldiisopinocampheylboranes (**2**, **3**),[5] methallyldiisopinocampheylborane (**4**),[6] 3,3-dimethylallyldiisopinocampheylborane (**5**),[7] *B*-isoprenyldiisopinocampheylborane (**6**),[8] [*Z*]-γ-alkoxyallyldiisopinocampheylborane (**7**),[9] and [(*E*)-γ-(1,3,2-dioxaborinanyl)allyl]diisopinocampheylborane (**8**).[10] Novel allylborating agents bearing functional groups in the allyl moiety have been developed by different research groups. Some of these are Barrett's *B*-[(*E*)-3-(diphenylamino)allyl]diisopinocampheylborane (**9**),[11] Oehlschlager's chloroallylborane reagent (**10**),[12] and Villieras's carbethoxyallylborane reagent (**11**).[13] *B*-2-Cyclohexen-1-yldiisopinocampheylborane (**12**)[14] also belongs to the family of allylborating agents.



1: X, Y, Z = H
2: X, Z = H, Y = Me
3: X, Y = H, Z = Me
4: X = Me, Y, Z = H
5: X = H, Y, Z = Me
6: X = vinyl, Y, Z = H
7: X, Z = H, Y = OMe
8: X, Y = H, Z = $B(OR)_2$
9: X, Y = H, Z = NPh_2
10: X, Y = H, Z = Cl



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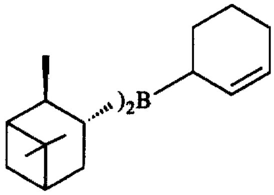

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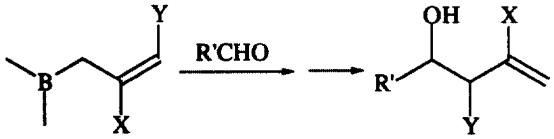
We decided to expand the scope of the allylboration procedure to include reagents of type **13** and **14** bearing an azido group, to prepare homoallylic alcohols bearing a 2- or 3- azido group (eq 1). These products would be valuable intermediates since the vinyl azide functionality can be readily transformed into amines, nitriles, azirines and ketones.[15] These should also be valuable for 1,3-dipolar cycloaddition reactions.[15]

PII: S0040-4039(98)02698-7

13: X = N$_3$, Y = H
14: X = H, Y = N$_3$

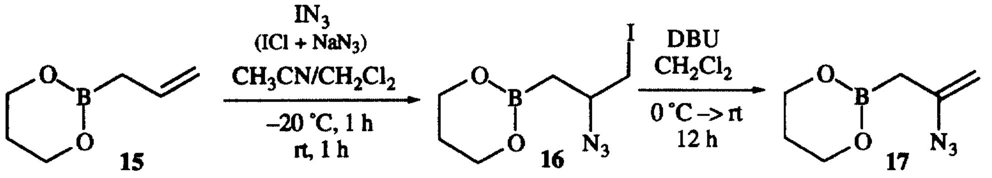


(1)

In addition, the diastereoselective reduction of the vinyl azide to the corresponding amine would provide valuable 1,2- and 1,3-amino alcohols. The importance of 1,3-difunctionalized compounds, especially 1,3-amino alcohols has been well documented. They are of special interest to organic chemists due to their presence in many natural products, such as amino sugars or aminopolyols[16] and antibiotics; e.g. Nikkomycine,[17] Negamicine,[18] etc. Accordingly, several methods, particularly those involving reductions, have been explored for their synthesis.[19] Our successful synthesis of 1-substituted 3-azido-3-propenols via an allylboration strategy is reported herein.

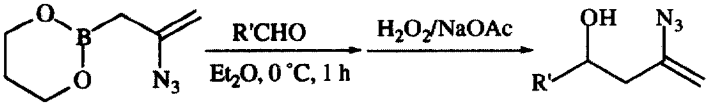
The regio- and stereoselective addition of halogen azides in the presence of polar solvents to simple olefins is well documented in the literature.[20] We applied the regioselective addition of iodine azide (IN$_3$: *Caution!*)[21], prepared *in situ* by the reaction of sodium azide and iodine monochloride, to the olefinic bond of the *B*-allyl-1,3,2-dioxaborinane **15** to achieve the synthesis of the new azidoallylboronate reagent **17**. Treatment of representative aldehydes with this reagent provided 3-azido-3-alken-1-ols (**18**) in high yields.

ICl was added to sodium azide in acetonitrile kept in an ice-methanol bath. *B*-Allyl-1,3,2-dioxaborinane[22] was added slowly to this with stirring. After the completion of the addition, the reaction mixture was stirred for 1 h, brought to ambient temperature, and stirred then for an additional hour. The dark colored supernatent solution was transferred to another flask, concentrated and extracted with pentane. Removal of pentane provided 3-azido-4-iodopropylboronate **16** in 70% isolated yield. The proton NMR (300 MHz) indicated a single regioisomer. Dehydroiodination of this intermediate to the required reagent **17** was achieved in quantitative yield by treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in dichloromethane (eq 2). The proton NMR showed two singlets at δ 4.75 and 4.80 ppm attributed to the vinylic protons.



(2)

Acetaldehyde was added to the azidoboronate **17** in ethyl ether at 0 °C. The reaction, followed by ^{11}B NMR spectroscopic analysis, was complete in 1 h. The usual H_2O_2 oxidative work up furnished 2-azido-1-penten-4-ol (**18a**) which was chromatographed over neutral alumina using 5% ethyl acetate in pentane as the eluant to obtain the pure material in 75% isolated yield. The generality of reagent **17** was demonstrated by treating several representative aldehydes, including an α,β-unsaturated aldehyde (*E*-crotonaldehyde). In all cases the corresponding 2-azido-1-alken-4-ols were isolated in 64-75% yields (eq 3). The ^1H NMR (300 MHz) of these azidoalcohols provides additional support to the fact that iodine azide added regeoselectively to the allylboronate, to give single regioisomer as indicated in eq 2.



17

18a: R' = Me, 75% **18d**: R' = Chx, 64%
18b: R' = *i*-Pr, 71% **18e**: R' = Ph, 70%
18c: R' = *t*-Bu, 68% **18f**: R' = (*E*)-Crt, 64%

(3)

This methodology provides a novel route for the synthesis of highly useful hydroxy substituted vinyl azides, promising 1,3-difunctionalized precursors for the synthesis of many valuable organic intermediates such as 1,3-amino alcohols, β-hydroxy ketones, etc.

In conclusion, we have demonstrated the successful utilization of the regioselective addition of iodine azide to the allylboronate with subsequent dehydrohalogenation to synthesize a new azidoallylboronate reagent in excellent yield. This reagent readily reacts with representative aldehydes, to provide, following hydrogen peroxide oxidation, synthetically useful 2-azido-1-alken-4-ols in good isolated yields. These can be readily converted to 1,3-amino alcohols, β-hydroxy ketones and several other important intermediates in heterocyclic chemistry. An asymmetric version of this reaction is also under way. We are also pursuing the diastereoselective reduction of the vinyl azide functionality using various reducing agents, such as lithium aluminum hydride,[23] borane, chloroborane, etc.

Attempts to prepare reagents of the type **14** have not succeeded thus far. The reaction of **15** with BrN_3 in the presence of light provided the corresponding 4-azido-3-bromo boronate in 80% yield and 100% regioisomeric purity. However, treatment with bases, such as Et_3N, DBU, $LiNChx_2$, etc. resulted in debromoboration. We are studying this reaction to achieve the dehydrobromination.

A representative experimental procedure for azidoallylboration follows. All operations were carried out under an inert atmosphere. Techniques for handling air- and moisture-sensitive materials have been previously described.[24] With the usual set-up, 50 mmol of NaN_3 was placed in 9 mL of acetonitrile in a 50 mL RB flask and cooled in an ice-methanol bath. To this ICl (22.6 mL of 1*M* in CH_2Cl_2) was added in 10 minutes and the reaction mixture was stirred for 15-20 min. *B*-allyl-1,3,2-dioxaborinane (2.52 g, 20 mmol) was then added and stirring continued at -15 °C for 1 h. The mixture was warmed to rt and stirred for an additional 1 h. The dark supernatant liquid was transferred to another flask and the precipitated solid was washed with Et_2O (3x15 mL). The combined material was concentrated and the residue was extracted with pentane and concentrated again to obtain 4.16 g (14 mmol, 70%) of **16** as a liquid. ^1H NMR (300 MHz) δ ($CDCl_3$) (ppm): 1.15 (dd, 2H, CH_2B), 1.95 (q, 2H, OCH_2CH_2), 3.3 (m, 2H, CH_2I), 3.7 (m, 1H, CHN_3), 4.0 (t, 4 H, $B(OCH_2)_2$.

DBU (1.8 mL, 15 mmol) was added slowly to the above compound in 12 mL of CH_2Cl_2 at rt and stirred overnight. The solvents were removed under aspirator and pentane added. The separated solid was washed with pentane and the combined pentane solution was concentrated to provide a quantitative yield (2.3 g, 14 mmol) of **17**. ^1H NMR (300 MHz) δ ($CDCl_3$) (ppm): 1.75 (s, 2H, CH_2B), 1.95 (m, 2H, OCH_2CH_2), 4.0 (t, 4 H, $B(OCH_2)_2$, 4.45 (s, 1H, =CHH), 4.55 (s, 1H, CHH). ^{13}C NMR δ ($CDCl_3$) (ppm): 27.23, 62.08, 98.00, 143.94. This material was used as such for the next step.

A solution of acetaldehyde (0.44 g, 10 mmol) in anhydrous Et_2O (50 ml) was added dropwise in 0.5 h to 1.84 g (11 mmol) of **17** in Et_2O and the reaction mixture was stirred at 0 °C for 1 h, until the reaction had been completed (^{11}B NMR shift from δ 32 to 18 ppm). Addition of methanol (1 ml) to this intermediate, followed by alkaline H_2O_2 oxidation, afforded a crude product which was chromatographed (ethyl acetate:hexane; 5:95 as eluent) to provide 0.90 g (71%) of **18a**. ^1H NMR (300 MHz) δ ($CDCl_3$) (ppm): 1.2 (d, 3H, CH_3), 2.2 (d, 2H, -CH_2-), 2.4 (s, 1H, OH), 3.95 (m, 1H, CHOH), 4.8 (d, 2H, =CH_2) ^{13}C NMR δ ($CDCl_3$) (ppm): 23.14, 43.90, 66.07, 100.82, 144.39.

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