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# *B*-Allenyl- and *B*-(Y-Trimethylsilylpropargyl)-10-phenyl-9-borabicyclo[3.3.2]-decanes: Asymmetric Synthesis of Propargyl and α-Allenyl 3°-Carbinols from Ketones

**Eliud Hernandez**, **Carlos H. Burgos**, **Eyleen Alicea**, and **John A. Soderquist***
*University of Puerto Rico, Department of Chemistry, Rio Piedras, PR 00931-3346*

## Abstract

Simple and efficient Grignard procedures are reported for the syntheses of *B*-allenyl-10-(phenyl)-9-borabicyclo[3.3.2]decane (1) and its *B*-(Y-trimethylsilylpropargyl)- counterpart (2) in both enantiomeric forms. Both add selectively to ketones providing propargyl- and α-silylallenyl 3°-carbinols, respectively (*i.e.*, 6 (61– 93% ee) and 9 (64–98% ee)). The air-stable boron by-product is efficiently recovered and recycled back to either 1 or 2. The ozonolysis and bromination of 9 provide non-racemic α-hydroxy acids and Y-bromopropynyl carbinols, respectively.

Recently, we reported the asymmetric allenyl- and propargylboration of aldehydes with the 10-trimethylsilyl-9-borabicyclo[3.3.2]decanes (10-TMS-9-BBDs).[1] These new reagents provide efficient syntheses of non-racemic propargylic and α-allenylic carbinols, respectively. Moreover, the robust, rigid and recyclable nature of the BBD ring system makes these systems highly attractive alternatives to other methods.[2] Neither process is known for prochiral ketones.[3] The success of these and related $S_E2'$ processes requires the formation of isomerically pure allenyl- or propargylborane reagents and Grignard procedures are now available for both. In related studies, we discovered that for asymmetric allylboration, the 10-TMS-9-BBD reagents are effective for aldehydes whereas the corresponding 10-Ph-9-BBD reagents are effective for ketones.[4] We now wish to report the preparation of both enantiomerically pure forms of *B*-allenyl-10-Ph-9-BBD (**1**) and γ-trimethylsilyl-propargyl-10-Ph-9-BBD (**2**) and their additions to prochiral ketones for the highly selective asymmetric syntheses of propargyl- (**5**) and α-allenyl- (**9**) 3°-carbinols, respectively.

The thermally stable (±)-*B*-MeO-10-Ph-9-BBD (**3**), readily prepared from *B*-MeO-9-BBN, serves as a very convenient precursor to both (+)-**4*S*** and (−)-**4*R*** as pure crystalline compounds with a combined total yield of 67%.[4] These complexes are air-stable and can be stored indefinitely. The reagents **1** were readily prepared in optically pure forms through the addition of allenylmagnesium bromide to the *N*-methylpseudoephedrine (NMPE) borinic ester complexes **4** (84%) (Scheme 1).[5] The Grignard reagent derived from 3-bromo-1-TMS-1-

jas@janice.uprr.pr.

Supporting Information Available: Full experimental procedures, analytical data and selected spectra for **1**, **2**, **6**, **9**–**13** and derivatives (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

propyne was also found to cleanly add to **4** to provide either (−)-**2*R*** or (+)-**2*S*** (97%) (Scheme 1).

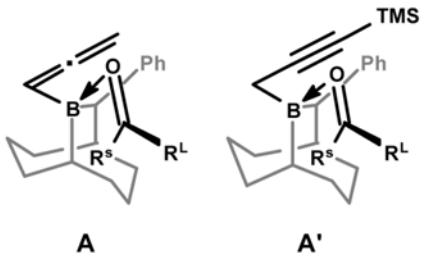
The asymmetric allenylboration of representative ketones was examined with **1**. Rapid reaction is observed with methyl ketones (3–12 h, −78 °C). The resulting 3°-carbinols **6** are obtained efficiently (62–85%) in high ee (61–93%) (Table 1). However, with propiophenone, the addition is much slower (2 d, 25 °C), with **5b** being produced in 76% ee. Notably, even very challenging substrates such as 2-butanone and methyl vinyl ketone give **6** with highly respectable levels of selectivities (*i.e.*, 74 (**c**) and 61% (**h**) ee, respectively).

Encouraged by these very positive results with the allenylboration of ketones with **1**, we turned our attention to the corresponding propargylboration of representative ketones with **2**. Based upon our earlier studies with the propargyl- vs allenylboration of aldehydes with the corresponding 10-TMS-9- BBD systems,[1] we expected even higher enantioselectivities from **2** than we had observed with **1**.

The asymmetric propargylboration of representative ketones and was examined with **2** in THF at −78 °C to obtain good to excellent yields (62–95%) of the corresponding α-allenyl 3°-carbinols **9** with methyl ketones generally exhibiting high selectivities (78–98% ee) (Table 2). Reaction times for these substrates varied considerably from 3–36 h for the methyl ketones. The aryl ketones containing electron-withdrawing groups (*i.e.*, Table 2, series **e**, **and f**) were the slowest in this group. Even less reactive is the ethyl ketone, propiophenone, whose propargylation requires 52 h at −78 °C. However, even highly demanding substrates such as 2-hexanone, give **9** with high selectivity (*i.e.*, **9b**, 84% ee).

The absolute stereochemistry for **9a** was determined by its conversion to the known atrolactic acid (**12**) through simple ozonolysis (Scheme 2). This oxidation is greatly facilitated by the α-TMS substitution in **9** which permits the ozonolysis to proceed directly to **11** through **10**.[1a] To discover other potential applications for this α-silylallenyl functionality, we examined the NBS-mediated bromodesilylation of **9a**,**j** together with two examples of *O*-Ac 2°-carbinols **9k**,**l**. The reactions are highly regioselective producing the corresponding propargyl bromides **13** cleanly in non-racemic form. This simple synthesis of these interesting polyfunctional compounds represents another useful feature of the TMS substitution[3b,c] in **2** which leads to **9**.

As previously described,[4] the 10-substituted-9-BBD ring clearly defines a “chiral pocket” as illustrated in the energetically favored pre-transition state complexes **A** and **A′** (see below) for the allenyl- and propargylboration processes with the reagents **1*R*** and **2*R***, respectively. Since BBD systems are stable, easily prepared in either enantiomerically pure form, highly reactive, environmentally friendly, recyclable and exhibit high selectivities over a wide range of unsymmetrical ketones, their applications to the asymmetric allenyl- and propargylboration to ketones represent highly useful new processes.




A A'

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgements

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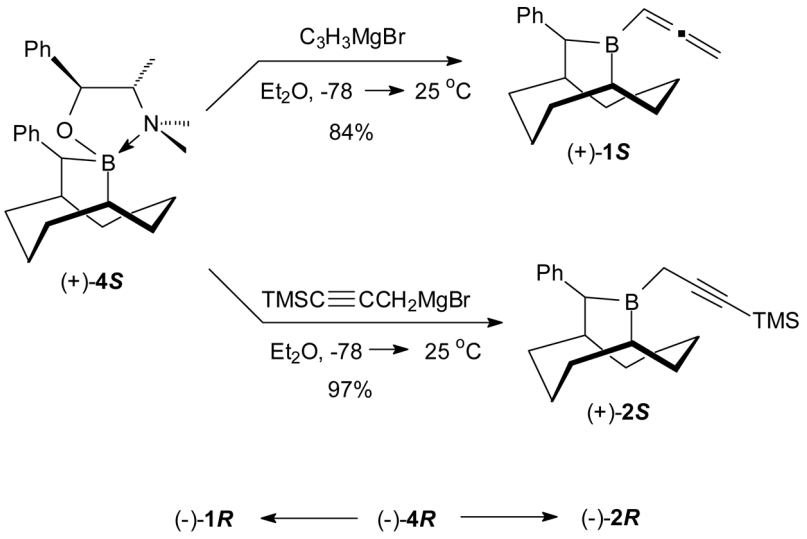
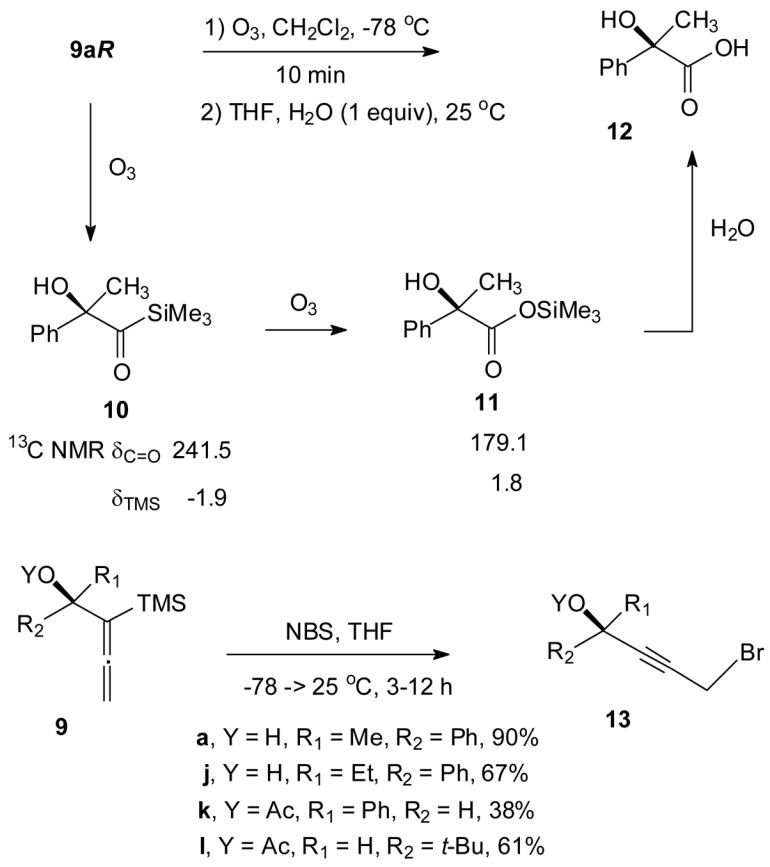


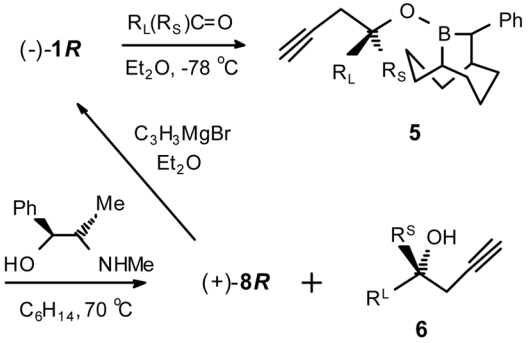

**Scheme 1.**




**Scheme 2.**

**Table 1**

Allenylboration of $R_LR_SCO$ with **1**



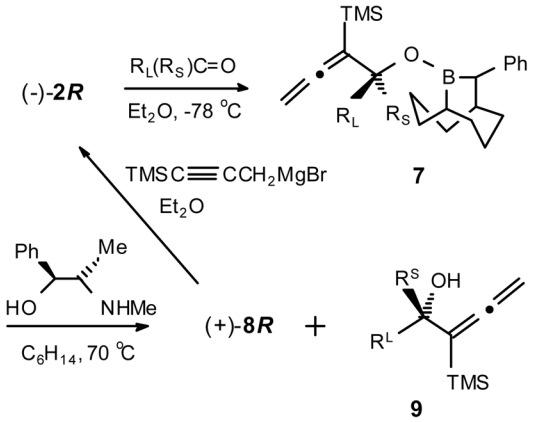

| $R_L$ | $R_S$ | **1** | **series** | **6(%)**[a] | **% ee**[b] **(abs config)** |
|---|---|---|---|---|---|
| Ph | Me | ***S*** | **a** | 74 | 91 (S) |
| Ph | Me | ***R*** | **a** | 85 | 93 (*R*) |
| Ph | Et | ***R*** | **b** | 65 | 76 (*R*) |
| Et | Me | ***R*** | **c** | 71 | 74 (*S*) |
| Bu | Me | ***S*** | **d** | 80 | 81 (*R*) |
| *i*-Pr | Me | ***R*** | **e** | 71 | 84 (*R*) |
| *t*-Bu | Me | ***S*** | **f** | 66 | 83 (*S*) |
| TMS | Me | ***S*** | **g** | 62 | 90 (*R*) |
| $CH_2$=CH | Me | ***S*** | **h** | 64 | 61 (*S*) |

[a] The **a** series was performed with both (−)-**1*R*** and (+)-**1*S***. The **a*S***, **b**, **f** and **h** series were conducted employing an oxidative work-up. For the remaining examples, the intermediate **5** was isolated and converted to **6** and either **4** or **8** was recovered (69–81%) *via* the NMPE work-up procedure.

[b] Product ee determined by conversion to the Alexakis esters[6] and analysis by $^{31}$P NMR.

**Table 2**

Propargylboration of $R_LR_SCO$ with **2**




| $R_L$ | $R_S$ | 1 | series | 9(%)[a] | % ee[b] (abs config)[c] |
|---|---|---|---|---|---|
| Ph | Me | ***S*** | **a** | 81 | 97 (*R*)[d] |
| Bu | Me | ***S*** | **b** | 62 | 84 (*R*) |
| *c*-$C_6H_9$ [e] | Me | ***S*** | **c** | 67 | 91 (*R*) |
| *p*-$MeOC_6H_4$ | Me | ***R*** | **d** | 95 | 92 (*S*) |
| *p*-$BrC_6H_4$ | Me | ***S*** | **e** | 80 | 98 (*R*) |
| *p*-$O_2NC_6H_4$ | Me | ***S*** | **f** | 79 | 98 (*R*) |
| 2-$C_4H_3S$[e] | Me | ***S*** | **g** | 71 | 78 (*S*) |
| 2-$C_4H_3O$[e] | Me | ***S*** | **h** | 82 | 80 (*R*) |
| Ph | Et | ***S*** | **i** | 63 | 64 (*R*) |

[a] In each case, the crystalline by-product **8** was recovered (50–85%) using a pseudoephedrine (PE) work-up (i.e., (1*R*,2*R*)-(−)-PE for (+)-8*S* and (1*S*,2*S*)-(+)-PE for (−)-**8*R***). This process is both more economical and convenient than with NMPE which is not currently available in both enantiomeric forms. Moreover, **8** is easily converted back to **2** (>95%) through the same general Grignard procedure used for **4**.

[b] Product ee was determined by reaction of **8** with phosphorus CDA and analysis by $^{31}P$ NMR.

[c] Configuration predicted by analogy to **9a**.

[d] Allenic alcohol **9a** was converted to the known 2-hydroxy-2-phenylpropionic acid and the sign of rotation was compared with the reported value.

[e] 1-cyclohexenyl, 2-thienyl and 2-furyl.