ORGANIC LETTERS

2004
Vol. 6, No. 23
4243−4244

Preparation of 5-Hydroxy-1-alkenyboronates from 1-Alkynylboronates, $Cp_2ZrCl_2/2EtMgBr$, and Aldehydes

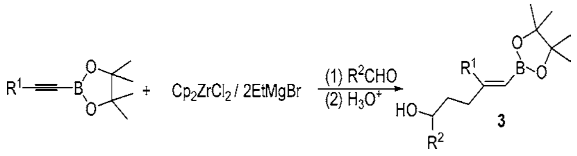
Abed Al Aziz Quntar and Morris Srebnik*

Department of Natural Products and Medicinal Chemistry, School of Pharmacy, Hebrew University in Jerusalem, Jerusalem 91120, Israel

msrebni@md.huji.ac.il

Received August 19, 2004

ABSTRACT



1-Alkynylboronates form five-membered zirconacycles with Cp_2ZrCl_2/2-EtMgBr as indicated by deuterium labeling. The zirconacycles add aldehydes to form seven-membered zirconacycles. Hydrolysis of the latter provides 5-hydroxy-1-alkenylboronates in fair to good isolated yields. Both aliphatic and aromatic aldehydes undergo insertion.

Vinylboronates are highly valued intermediates in organic synthesis.[1] They are available in a highly regio- and stereoselective manner by hydroboration and other protocols.[2] The ease with which they undergo transmetalation[3] has enabled the introduction of carbon−carbon double bonds in complex molecules. The advent of the Suzuki−Miyaura[4] coupling protocol has considerably increased their importance. We have been interested in the preparation of vinylboronates by reaction of zirconocene reagents with alkynylboronates. Hydrozirconation of 1-alkynylboronates with Schwartz's reagent (Cp_2ZrHCl) provides intermediates that can be converted into highly functionalized vinylboranes.[5] The use of the Negishi reagent (Cp_2ZrCl_2/2*n*-BuLi) with 1-alkynylboronates, on the other hand, leads to 1,3-butadienes, the result of homocoupling.[6] The reagent Cp_2ZrCl_2/2-EtMgBr behaves differently from the above two reagents.[7] It is known to give a five-membered zirconacycle. Addition of alkynylboronates to the reagent Cp_2ZrCl_2/

---

[1] (a) Pelter, A.; Smith, K.; Brown, H. C. *Borane Reagents*; Academic Press: New York, 1988. (b) Suzuki, A. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F, Stang, P. J., Eds.; VCH: Weinheim, 1988; p 49. (c) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633−9695.

[2] (a) Smith, K.; Pelter, A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds; Pergamon Press: Oxford, 1991; Vol. 8, p 703.

[3] Some examples are as follows. Boron−zinc: (a) Srebnik, M. *Tetrahedron Lett.* **1991**, *32*, 2449. (b) Hupe, E.; Calaza, M. I.; Knochel, P. *J. Organomet. Chem.* **2003**, *60*, 136−142. Boron−copper: (c) Miyaura, N.; Itoh, M.; Suzuki, A. *Tetrahedron Lett.* **1976**, 255. Boron−silicon: (c) Singleton, D. A.; Leung, S.-W. *J. Organomet. Chem.* **1997**, *544*, 157−161 and references cited therein. Boron−zirconium: (d) Quintanilla, R.; Cole, T. E. *Tetrahedron* **1995**, *51*, 4297−4308. Boron−lithium: (e) Kawachi, A.; Minamimoto, T.; Tamao, K. *Chem. Lett.* **2001**, 1216−1217. Boron−tin: (f) Nöth, H.; Vahrenkamp, H. *J. Organomet. Chem.* **1968**, *11*, 399. (g) Eisch, J. J.; Kotowicz, B. W. *Eur. J. Inorg. Chem.* **1998**, 761−769. (h)-Sashida, H.; Kuroda, A. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1965−1969.

[4] (a) Miyaura, N. *Top. Curr. Chem.* **2002**, *219*, 11−52. (b) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633−9695.

[5] (a) Zheng, B.; Srebnik, M. *J. Organomet. Chem.* **1994**, *474*, 49−53. (b) Deloux, L.; Skrzypczak-Jankun, E.; Cheesman, B. V.; Sabat, M.; Srebnik, M. *J. Am. Chem. Soc.* **1994**, *116*, 10302−103023. (c) Deloux, L.; Srebnik, M. *J. Org. Chem.* **1994**, *59*, 6871−6873. (d) Zheng, B.; Srebnik, M. *J. Org. Chem.* **1995**, *60*, 3278−3279. (e) Deloux, L.; Srebnik, M. *J. Org. Chem.* **1995**, *60*, 3276−3277. (f) Pereira, S.; Srebnik, M. *Organometallics* **1995**, *14*, 3127−3127−3128. (g) Pereira, S.; Srebnik, M. *J. Org. Chem.* **1995**, *60*, 4316−4217. (h) Zheng, B.; Srebnik, M. *Synth. Commun.* **1996**, *26*, 393−396. (i)) Deloux, L.; Srebnik, M. *Tetrahedron Lett.* **1996**, *37*, 2735−2738.

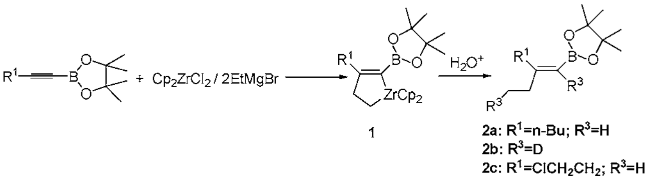
[6] Desurmont, G.; Klein, R.; Uhlenbrock, S.; Laloë,E.; Deloux, L.; Giolando, D. M.; Yong Wah Kim, Y.W.; Pereira, S.; Srebnik, M. *Organometallics* **1996**, *15*, 3323−3328.

[7] (a) Takahashi, T.; Suzuki, N.; Kageyama, M.; Nitto, Y.; Saburi, M.; Negishi, E. *Chem. Lett.* **1991**, 1579−1582. (b) Takahashi, T.; Nitto, Y.; Seki, T.; Saburi, M.; Negishi, E. *Chem. Lett.* **1990**, 2259−2262.

10.1021/ol0483504 CCC: $27.50

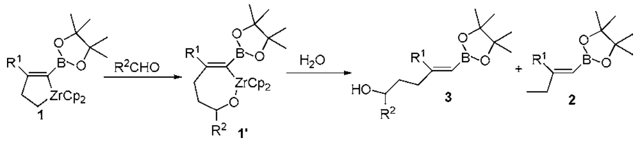
2EtMgBr smoothly produced the zirconacyclopentenes **1** which, upon hydrolysis, afforded (*Z*)-2-(2-ethylhex-1-enyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **2a** in 85% isolated yield (Scheme 1). Deuterium labeling of the intermediate **1** by D_2O workup of the reaction mixture indicates the presence of two deuterium atoms in the **2b**, which is indicative of two metal carbon bonds in **1**.

Scheme 1



A new class of vinylboronates **3** were obtained in a regioselective manner by addition of aldehydes to the intermediate **1** (Scheme 2). Insertion presumably produces a seven-membered ring zirconacycle[8] **1′** which, after hydrolysis, provided product **3** in moderate isolated yields. The vinylboronates **3** are stable, oily compounds which were extracted from the reaction mixture by diethyl ether, isolated by silica gel chromatography, and characterized by GCMS, ^1H, ^{11}B, and ^{13}C NMR, and elemental analysis.

Scheme 2



Optimization of **3** (Table 1) revealed that while it is possible to increase the isolated yield substantially by increasing the number of equiv of aldehyde to five, reasonable yields could be obtained with only 2 equiv. This was adopted in all cases. The optimal temperature was 50 °C. All efforts to raise the yields by heating the reaction mixture at >50 °C for longer times were unsuccessful.

The reaction was general (Table 2) and proceeded with aliphatic aldehydes and substituted and nonsubstituted aromatic aldehydes. Moreover, both alkynylboronates, 2-(hex-1-ynyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane as well as 2-(5-chloropent-1-ynyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, successfully produced the desired products **3a**−**e** and **3f**−**h**, respectively. The yields were varied (43−58%), and the reaction was always accompanied by the side product **2a** or **2c**, which is indicative that part of the zirconacyclopentenes **1** did not add aldehyde to form the zirconacycloheptenes **1′**.

Table 1. Optimization of Conditions for Obtaining **3a**

equiv of PhCHO	*T* (°C)	isolated yield, %
1	25	32
2	25	53
2	50	58
2	75	58
3	25	61
5	25	73
2	50	75

Table 2. Synthesis of Compounds **3**

products **3**	R^1	R^2	$^{11}B,\delta^a$	yield,[b] % (^{11}B)[c]
a	*n*-Bu	Ph	30.5	58 (68)
b	*n*-Bu	*p*-CH_3Ph	31.1	53 (68)
c	*n*-Bu	*p*-CH_3OPh	29.9	58 (65)
d	*n*-Bu	Me	30.1	55 (65)
e	*n*-Bu	Et	30.0	50 (58)
f	Cl-*n*-Pr	Ph	30.1	45 (60)
g	Cl-*n*-Pr	*m*-CH_3Ph	30.2	47 (56)
h	Cl-*n*-Pr	*p*-CH_3OPh	30.7	43 (53)

[a] In $CDCl_3$. [b] Isolated yield after silica gel chromatography. [c] Yield based on ^{11}B NMR.

The regioselectivity was determined by NMR data. The presence of a singlet in the double bond region (5.11−5.21 ppm), in addition to the splitting of the hydrogen on the alcoholic carbon (3.79−4.68 ppm) by the hydrogens of C4, are indicative that the coupling of the aldehyde was on C4 to boron. On the other hand, the ^{11}B NMR chemical shift in the region (29.86−31.06 ppm) is appropriate to vinylboronate products.

Acknowledgment. We thank the Israeli Science Foundation for support of this work. A.A.A.Q. thanks The Faculty of Medicine for a postdoctoral fellowship.

Supporting Information Available: Full experimental protocol and spectroscopic and analytical data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL0483504

---

[8] Copéret, C.; Negishi, E.; Xi, Z.; Takahashi, T. *Tetrahedron Lett.* **1994**, *35*, 695−698.