



Diastereoselective synthesis and reactions of diorganozinc reagents obtained after hydroborations with 9-BBN-H, thexylborane and catecholborane

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Received 28 August 2001; accepted 12 October 2001

Abstract—The scope of organoboranes can be greatly enhanced by a boron–zinc exchange reaction, providing organozincs that react with a broad range of electrophiles. Diastereomerically enriched diorganozincs can be obtained after hydroborations with 9-BBN-H, thexylborane and catecholborane. © 2001 Elsevier Science Ltd. All rights reserved.

Organozinc reagents are very useful organometallic reagents. Many polyfunctional organozinc compounds can be prepared¹ and used efficiently for the formation of new carbon–carbon bonds in the presence of copper(I)² and palladium(0)³ catalysts. Furthermore, the carbon–zinc bond of secondary alkylzinc reagents (except of benzylic zinc reagents) displays a high configurational stability. This property prompted us to investigate a general method for the preparation of chiral secondary alkylzinc compounds. We have demonstrated that a hydroboration/boron–zinc exchange sequence allows access to a broad range of these chiral organometallic species.⁴ Unfortunately, so far only diethylalkylboranes could be converted to organozinc reagents in satisfactory yields. This is a strong limitation, since with many olefins Et_2BH undergoes hydroboration only with moderate diastereoselectivities. More bulky hydroborating reagents give usually far better results.

Herein, we wish to report that the use of $i\text{Pr}_2\text{Zn}$ instead of Et_2Zn ⁵ allows the direct transmetalation of various primary organoboranes and boronic esters to the corresponding organozinc reagents (Method A). For secondary organoboranes and boronic esters, a two-step transmetalation of the organoborane/boronic ester to a diethylalkylborane, followed by a boron–zinc exchange with $i\text{Pr}_2\text{Zn}$ was applied (Method B). Thus, the hydro-

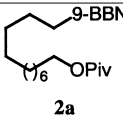
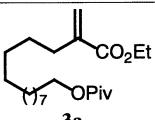
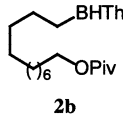
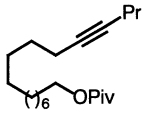
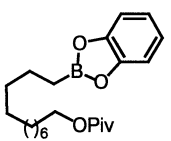
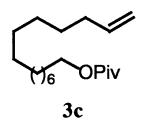
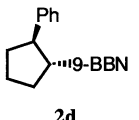
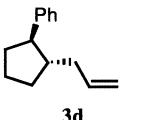
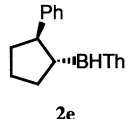
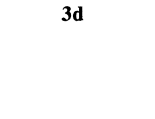
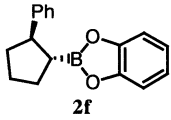
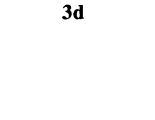
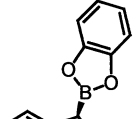
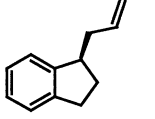
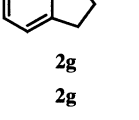
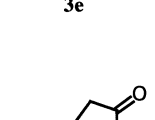

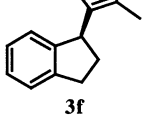
boration of 10-undecenyl pivalate (**1a**) with 9-BBN-H (2 equiv., rt, 12 h) provides the corresponding organoborane **2a**, which, after treatment with $i\text{Pr}_2\text{Zn}$ (5 equiv., rt, 4 h, Method A), transmetalation with $\text{CuCN}\cdot 2\text{LiCl}$ ⁶ and allylation with ethyl 2-(bromomethyl)acrylate, furnishes the desired product **3a** in 66% yield (entry 1 of Table 1). Similarly, the hydroboration of **1a** with thexylborane⁷ (ThBH_2) (2 equiv., -30°C to rt, 12 h) leads to the organoborane **2b**. Reaction of **2b** with $i\text{Pr}_2\text{Zn}$ (5 equiv., rt, 5 h) cleanly provides the corresponding organozinc reagent, which after transmetalation with $\text{CuCN}\cdot 2\text{LiCl}$ (1.5 equiv., -78°C , 30 min) and reaction with 1-bromopentyne (5 equiv., -40°C , 36 h) provides the desired alkyne **3b** in 52% overall yield (entry 2, Table 1). Finally, the rhodium-catalyzed hydroboration of **1a** with catecholborane (1.1 equiv., 0°C to rt, 5 h) in the presence of $\text{RhCl}(\text{PPh}_3)_3$ (2 mol%)⁷ furnishes the boronic ester **2c**. Subsequent transmetalation with $i\text{Pr}_2\text{Zn}$ (10 equiv.) requires 36 h at 25°C and leads, after a copper(I)-mediated allylation, to the desired product **3c** in 58% yield (entry 3 of Table 1). These results indicate that primary functionalized organoboranes are readily converted to the corresponding organozinc species. Similar results are obtained with secondary organoboranes. Thus, the hydroboration of 1-phenylcyclopentene (**1b**) with either 9-BBN-H, ThBH_2 or catecholborane (in the presence of $[\text{Rh}(\text{COD})_2]\text{BF}_4$, 3 mol%)⁸ furnishes the corresponding organoboranes **2d–f**. After reaction with Et_2BH (5 equiv., 50°C , 16 h) and $i\text{Pr}_2\text{Zn}$ (5 equiv., rt, 5 h) (Method B), the resulting secondary diorganozinc species can be allylated with high retention of the *trans*-stereochemistry (93–95% *trans*; entries 4–6 of Table 1). Benzylic zinc reagents can also be generated. Thus, the

Keywords: hydroboration; transmetalation; boron–zinc exchange; zinc organometallics.

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Rh-catalyzed hydroboration of indene (**1c**) with catecholborane⁸ leads to the boronic ester **2g**. The corresponding benzylic zinc reagent is obtained after a treatment with Et₂BH and *i*Pr₂Zn (Method B). This

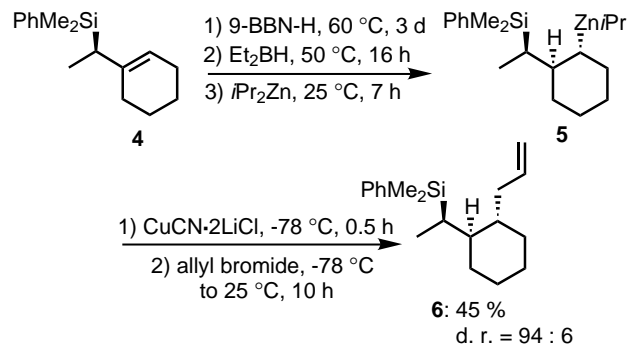
Table 1. Products obtained by copper(I)-mediated reactions of diorganozinc reagents obtained by a boron–zinc exchange reaction

Entry	Organoborane of Type 2	Method	Product of Type 3	Yield (%) ^a
1	 2a	A	 3a	66
2	 2b	A	 3b	52
3	 2c	A	 3c	58
4	 2d	B	 3d	58
5	 2e	B	 3d	61
6	 2f	B	 3d	58
7	 2g	B	 3e	54
8	 2g	B	 3f	58
9	 2g	B	 3g	51

^aIsolated yield of analytically pure compound. Piv = pivalate; ThBH = thexylborane; 9-BBN = 9-borabicyclo[3.3.1]nonane.

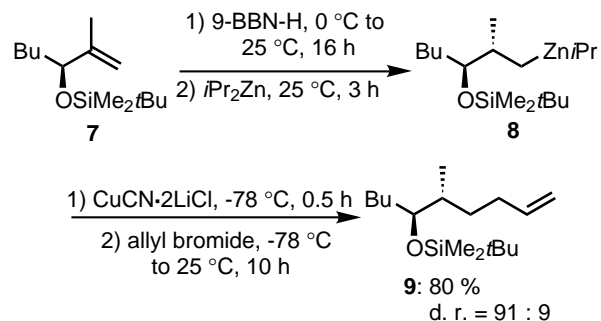
organozinc reagent then undergoes copper-mediated reactions with allyl bromide, 3-iodo-2-methylcyclopent-2-en-1-one and propionyl chloride. The expected products **3e–g** are obtained in 51–58% yield (entries 7–9 of Table 1).¹² This transmetalation of boronic esters, obtained by a Rh-catalyzed hydroboration, considerably broadens the scope of the classical hydroboration reaction, allowing now not only the usual oxidation of the boronic ester with H₂O₂ leading to an alcohol, but also the quenching with various carbon electrophiles.

With this method in hands, diastereoselective syntheses of zinc organometallics can be readily achieved. In contrast to Et₂BH, the more sterically hindered ThBH₂, 9-BBN-H and catecholborane allow highly diastereoselective hydroborations.⁹ Fleming et al. reported excellent diastereoselectivities for hydroborations of a variety of different allylsilanes using 9-BBN-H.¹⁰ Thus, the hydroboration of **4** with 9-BBN-H (2 equiv., 60°C, 3 days) provides, after treatment with Et₂BH (5 equiv., 50°C, 16 h) and reaction with *i*Pr₂Zn (5 equiv., rt, 7 h), the silylated organozinc reagent **5**, which, after Cu(I)-mediated allylation, gives the silyl derivative **6** with a diastereoselectivity of 94:6 in 45% overall yield (Scheme 1).



Scheme 1.

Still et al. showed that silylated allylic alcohols are diastereoselectively hydroborated with 9-BBN-H.¹¹ Applying the reported conditions for the hydroboration with 9-BBN-H (3 equiv., 0°C to rt, 16 h) and after a subsequent B–Zn exchange (4 equiv. *i*Pr₂Zn, 25°C, 4 h) the *anti*-diastereoisomer **8** was obtained in good diastereoselectivities (d.r.=91:9). The copper-mediated reaction of **8** provided the desired *anti*-alcohol derivative **9** in good yield (Scheme 2).



Scheme 2.

In conclusion, we have shown that a range of primary and secondary organoboranes can be readily transmetallated to the corresponding organozinc species by treatment with an excess of $i\text{Pr}_2\text{Zn}$. This method allows access to new diastereomerically enriched organozinc compounds, which react in acceptable yields with various electrophiles. Further applications to the preparation of chiral organozinc reagents are currently underway.

Acknowledgements

We thank the DFG (Leibniz-Program) for financial support. E.H. thanks the Fonds der Chemischen Industrie for a Kekulé-fellowship. M.I.C. thanks the European Community for a Marie Curie fellowship (HPMF-CT-2000-01024). We thank Chemetall GmbH (Frankfurt), BASF AG and Degussa AG (Hanau) for generous gifts of chemicals.

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- Typical procedure: preparation of 3-(2,3-dihydro-1H-inden-1-yl)-2-methyl-2-cyclopenten-1-one (**3f**): A flame-dried 25 mL flask equipped with a magnetic stirring bar, an argon inlet and a septum was charged with $[\text{Rh}(\text{COD})_2]\text{BF}_4$ (0.03 mmol, 0.03 equiv., 12 mg) and 1,4-bis(diphenylphosphino)-butane (0.03 mmol, 0.03 equiv., 13 mg). THF (1 mL) was added and the mixture stirred for 30 min at 25°C. Indene (116 mg, 1.0 mmol, 1.0 equiv.) and catecholborane (1.2 mmol, 1.2 equiv., 144 mg) were added and the solution was stirred at room temperature overnight. After pumping off the volatiles (0.1 mmHg, 50°C, 3 h), Et_2BH (0.69 mL, 5.0 mmol, 5 equiv., 7.3 M in Me_2S) was added and the resulting mixture was stirred for 16 h at 50°C. After pumping off the volatiles (0.1 mmHg, 25°C, 2 h), $i\text{Pr}_2\text{Zn}$ (1.0 mL, 5.0 mmol, 5 equiv., 5.0 M in Et_2O) was added and the mixture was stirred 5 h at 25°C. The volatiles were pumped off (0.1 mmHg, 25°C, 0.5 h), the grey-black residue was diluted with THF (2 mL) and cooled to –78°C. A freshly prepared solution of $\text{CuCN}\cdot 2\text{LiCl}$ (1.5 mL, 1.5 mmol, 1.5 equiv., 1 M in THF) was slowly added over 40 min via syringe pump and the mixture stirred for 30 min at –78°C. Then, 1-methyl-2-iodo-cyclopenten-1-one (1.11 g, 5 mmol, 5 equiv.) in THF (1 mL) was slowly added (40 min) via syringe pump. The mixture was stirred for 16 h at –40°C. The reaction mixture was then poured into a saturated aqueous NH_4Cl solution (150 mL) containing NH_3 (aq) (2 mL, 30% in H_2O). After extraction with Et_2O (3×150 mL) the combined organic phases were dried over MgSO_4 . The solvent was removed and the crude product purified by column chromatography (SiO_2 ; hexanes/ Et_2O =90:10) affording **3f** as a colorless oil (123 mg, 0.58 mmol, 58% yield).