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9-Borabicyclo[3.3.1]nonane (9-BBN) in Organic Synthesis

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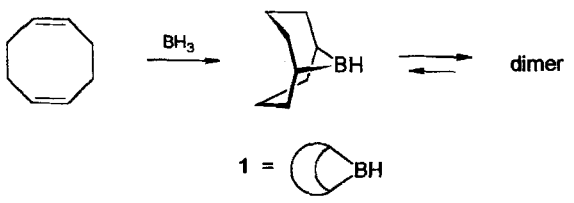
1 Introduction

Boranes are known for a few decades as valuable reagents for the hydroboration of alkenes and the reduction of various functional groups. However, the commonly used borane (BH_3·THF) suffers from difficulties because of its polyfunctional nature and relatively low selectivity in certain cases. These problems can be overcome by the use of dialkylboranes as 9-borabicyclo[3.3.1]nonane (9-BBN, **1**), disiamylborane (bis(1,2-dimethylpropyl)borane), and dicyclohexylborane. These reagents are more selective than borane itself as a result of steric and electronic effects together with a diminution of reaction possibilities through the availability of only a single B–H bond [1]. Of all the dialkylboranes 9-BBN has found widest application in organic synthesis. 9-BBN is prepared by hydroboration of 1,5-cyclooctadiene with borane and exists as a dimer [2] (Scheme 1). It is marketed as a pure solid which is remarkably stable at room temperature when stored under an inert atmosphere. Solutions in THF and hydrocarbons are also commercially available. Reactions occur significantly faster in THF than in hydrocarbons, since in THF the 9-BBN dimer is in equilibrium with the more reactive 9-BBN·THF complex [1].



Scheme 1

The earlier applications of 9-BBN in hydroborations and reductions are well documented [1–3]. Therefore, this article mainly focusses on topical applications of this reagent.

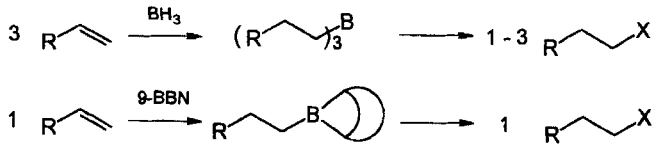
2 Reductions

In contrary to the hydridoborates (e.g. $NaBH_4$) which are *nucleophilic* hydride donors, 9-BBN and other trivalent boranes are *electrophilic* reducing agents. This difference in the reaction mechanisms causes different reactivities of certain functional groups against these two types of reducing agents. A tabular survey over the behaviour of numerous functional groups against 20 boron containing reagents is given in ref. [1].

9-BBN reduces aldehydes and ketones rapidly to the corresponding alcohols in the presence of almost any other functional group [4]. This is complementary to the behaviour of borane, which exhibits greatest reactivity towards olefins and carboxylic acids. Vinylogous aldehydes and ketones are selectively reduced to allylic alcohols [5]. On the other hand, hydroboration of *aryl* 1-alkenylketones with 9-BBN proceeds in a 1,4-fashion to give boron (Z)-enolates. These can be hydrolyzed to saturated aryl alkylketones or treated with aldehydes to give *syn*-aldols [6]. The smooth reduction of acid chlorides to alcohols by 9-BBN was quite unexpected since borane and disiamylborane are inert to acid chlorides. Further, it should be pointed out that *N,N*-disubstituted amides are reduced to alcohols by 9-BBN, whereas reaction with borane gives tertiary amines and with disiamylborane gives aldehydes. Carboxylic acids are slowly reduced to primary alcohols by 4 equ. of 9-BBN in refluxing THF [4]. Recent research showed that sodium and lithium salts of carboxylic acids are readily converted to aldehydes by 2 equ. of 9-BBN at room temperature [7]. Both aliphatic and aromatic nitro compounds, disulfides, sulfones, tosylates, and halogen compounds are inert to 9-BBN under standard conditions [4].

3 Hydroboration of Double and Triple Bonds and Subsequent Functionalization

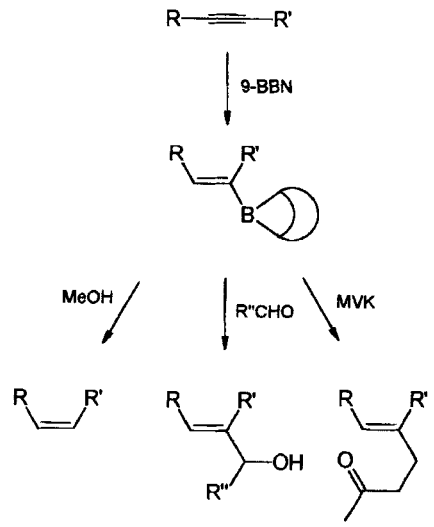
The hydroboration of olefins with borane and its derivatives proceeds in an *anti*-Markovnikov manner. The resulting trialkylboranes can be converted to various functional groups. Many of the reactions of trialkylboranes result in the utilization of only *one* group on boron. Consequently, for the conversion of a valuable alkene, the yield may be limited to 33%. In many cases, the alkyl group in a *B*-9-alkyl-BBN derivative reacts preferentially, providing a much higher yield based on alkene [3] (Scheme 2).



Scheme 2

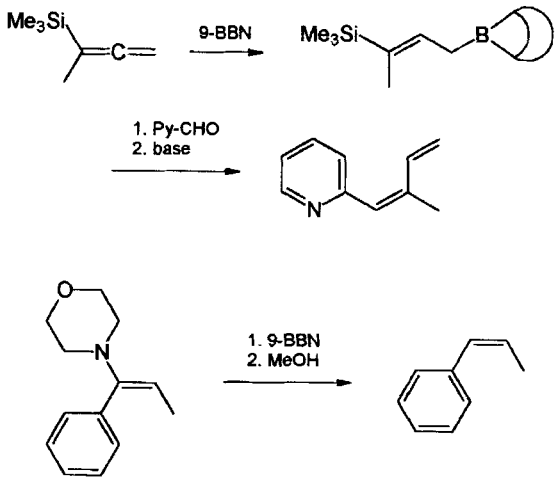
Another advantage of 9-BBN is its extremely high regioselectivity in hydroborations. Terminal alkenes give the terminal organoborane almost exclusively. The regioselectivity of 9-BBN is higher than that of disiamylborane and much higher than that of BH_3·THF [8]. Oxidation of *B*-alkyl-9-BBN derivatives with H_2O_2/NaOH gives alcohols, oxidation with SO_3-pyridine complex [9] the corresponding aldehydes. Treatment with Br_2/NaOMe [10] gives alkyl bromides, and cyanation with NaCN/$Pb(OAc)_4$ [11] or CuCN/$Cu(OAc)_2$/$Cu(acac)_2$ [12] leads to nitriles. Carbonylation with CO/$LiAlH(OMe)_3$ gives, depending on work-up conditions, homologous aldehydes or primary alcohols [13]. The alkyl chain of *B*-alkyl-9-BBN derivatives can be elongated by two or more carbon atoms by reaction with α-haloesters, -nitriles or -ketones in the presence of base [1,14].

Alkynes react slower with 9-BBN than alkenes do. While terminal alkynes can give mixtures of 1,1-diborylalkanes and vinylboranes, hydroboration of internal alkynes with stoichiometric amounts of 9-BBN gives (*Z*)-vinylboranes. The regioselectivity of this reaction is governed by both steric and electronic effects [1]. The *B*-vinyl-9-BBN derivatives are readily protonolyzed to (*Z*)-alkenes by methanol [15]. Reaction with aldehydes gives allylic alcohols [16], and conjugate addition to enones yields γ,δ-unsaturated ketones [17] (Scheme 3).



Scheme 3

With few exceptions the 9-BBN hydroboration of allenes results in the attack of boron at the end carbons of the allene moiety giving *B*-allyl-9-BBN derivatives. Hydroboration of a trimethylsilyl allene followed by reaction with aromatic aldehydes and base-induced Petersen olefination gave aryl 1,3-butadienes [18]. Addition of 9-BBN to enamines followed by methanolysis gave olefins with high stereoselectivity. Hydroboration of the same enamines with borane dimethyl sulfide complex followed by methanolysis and oxidative work-up lead to the isomeric olefins [19] (Scheme 4).



Scheme 4

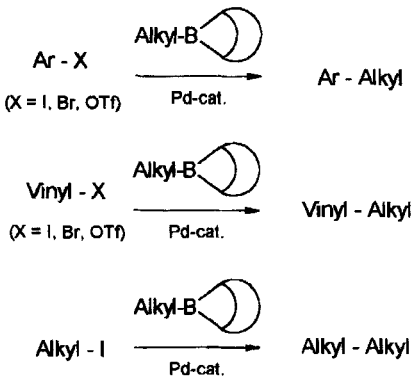
4 Palladium-Catalyzed Transformations of 9-BBN Derivatives

In 1989 Suzuki and co-workers [20] found that the Pd-catalyzed cross-coupling reaction of *in situ* prepared primary *B*-alkyl-9-BBN derivatives with haloarenes or vinyl halides gave the corresponding alkylarenes or alkyl olefins. Thus, primary alkyl groups on boron are transformed more readily than the carbons of the bicyclic part. So the 9-BBN hydroboration/cross-coupling sequence provides a very effective one-pot method for the alkylation of arenes with complete utilization of the olefin (simple trialkylboranes transfer only *one* alkyl group!). Later it was found that *B*-alkyl- and *B*-alkenyl-9-BBN derivatives can also be used for cross-coupling reactions with aryl and vinyl triflates [21] and that even alkyl-alkyl couplings are possible with primary alkyl iodides [22] (Scheme 5).

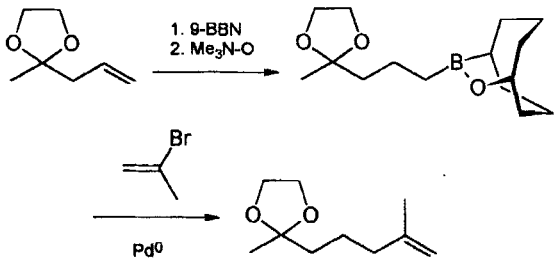
The yield of the products may be enhanced by first oxidizing the *B*-alkyl-9-BBN skeleton with trimethylamine *N*-oxide to a cyclic borinate ester and then performing the coupling reaction [23] (Scheme 6).

In the cross-coupling with vinyl and aryl triflates reductive removal of the trifluoromethanesulfonyloxy group by excess 9-BBN to give an alkene or arene may become a severe side reaction [24]. This problem can be circumvented by addition of water after the hydroboration of the olefin.

Some recent examples for the application of 9-BBN in Pd-catalyzed cross-coupling reactions are shown in Scheme 7. Thus, olefins can be converted to aldehydes or ketones with chain elongation by hydroboration, coupling reacton with enol ethers or enol esters of α-bromo carbonyl compounds and subsequent acidic hydrolysis [25]. Unsymmetrical 1,2-diarylethanes can be prepared from two aryl bromides by a



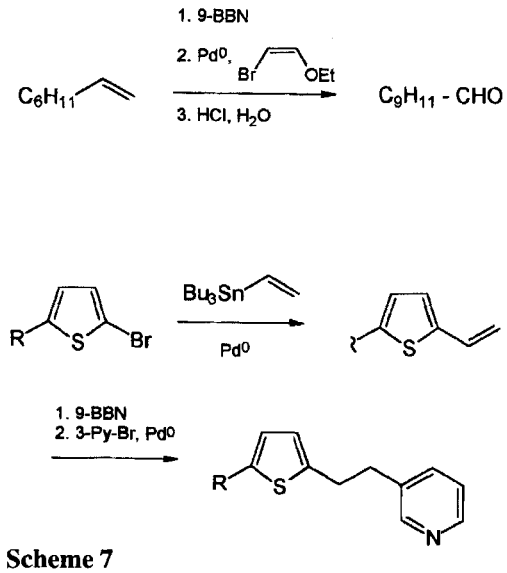
Scheme 5



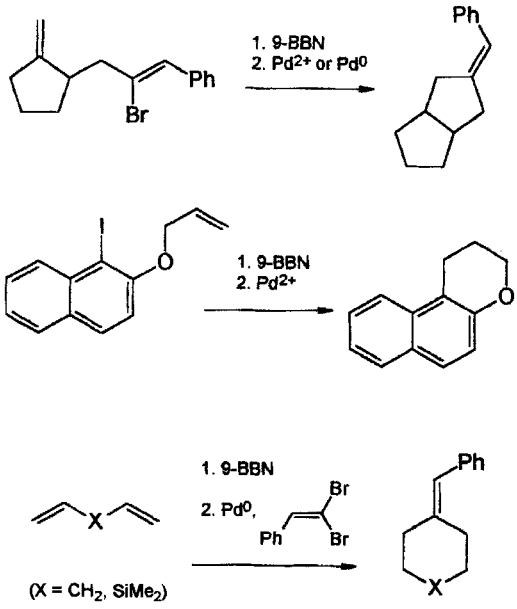
Scheme 6

sequence involving two Pd-catalyzed coupling reactions, one of them utilizing 9-BBN [26].

There are even some examples for the application of 9-BBN hydroboration/cross-coupling to the synthesis of cyclic compounds. However, this intramolecular coupling reaction is restricted to the preparation of five- and six-membered rings [20, 22, 27]. Starting from a diene and a 1,1-dibromoalkene, this methodology has also been applied to a double coupling reaction to give semicyclic olefins [28] (Scheme 8).



Scheme 7



Scheme 8

References

[1] A. Pelter, K. Smith, H. C. Brown, Borane Reagents, Academic Press, London 1988

[2] a) H. C. Brown, E. F. Knights, C. G. Scouten, J. Am. Chem. Soc. **96** (1974) 7765; b) J. A. Soderquist, A. Negron, Org. Synth. **70** (1992) 169

[3] H. C. Brown, C. F. Lane, Heterocycles **7** (1977) 453

[4] H. C. Brown, S. Krishnamurthy, N. M. Yoon, J. Org. Chem. **41** (1976) 1178

[5] S. Krishnamurthy, H. C. Brown, J. Org. Chem. **42** (1977) 1197

[6] Y. Matsumoto, T. Hayashi, Synlett **1991**, 349

[7] J. S. Cha, S. Y. Oh, K. W. Lee, M. S. Yoon, J. C. Lee, J. E. Kim, Heterocycles **27** (1988) 1595

[8] H. C. Brown, E. F. Knights, C. G. Scouten, J. Am. Chem. Soc. **96** (1974) 7765

[9] M. Matsumoto, N. Watanabe, E. Mori, M. Aoyama, J. Kusunoki, T. Yamaura, Heterocycles **38** (1994) 2589

[10] H. C. Brown, C. F. Lane, Tetrahedron **44** (1988) 2763

[11] Y. Masuda, M. Hoshi, T. Yamada, A. Arase, J. Chem. Soc., Chem. Commun. **1984**, 398

[12] Y. Masuda, M. Hoshi, A. Arase, J. Chem. Soc., Chem. Commun. **1989**, 266

[13] H. C. Brown, E. F. Knights, R. A. Coleman, J. Am. Chem. Soc. **91** (1969) 2144

[14] M. M. Midland, Y. C. Kwon, J. Org. Chem. **46** (1981) 229

[15] H. C. Brown, G. A. Molander, J. Org. Chem. **51** (1986) 4512

[16] P. Jacob, H. C. Brown, J. Org. Chem. **42** (1977) 579

[17] P. Jacob, H. C. Brown, J. Am. Chem. Soc. **98** (1976) 7832

[18] P. D. Sattsangi, K. K. Wang, Tetrahedron Lett. **33** (1992) 5025
[19] B. Singaram, C. T. Goralski, M. V. Rangaishenvi, H. C. Brown, J. Am. Chem. Soc. **111** (1989) 384
[20] N. Miyaura, T. Ishiyama, H. Sasaki, M. Ishikawa, M. Satoh, A. Suzuki, J. Am. Chem. Soc. **111** (1989) 314
[21] T. Ishiyama, S. Abe, N. Miyaura, A. Suzuki, Chem. Lett. **1992**, 691
[22] T. Oh-e, N. Miyaura, A. Suzuki, J. Org. Chem. **58** (1993) 2201
[23] B. Santiago, J. A. Soderquist, J. Org. Chem. **57** (1992) 5844
[24] a) K. Kondo, M. Sodeoka, M. Shibasaki, J. Org. Chem. **60** (1995) 4322; b) F. Bracher, B. Schulte, publication in preparation
[25] S. Abe, N. Miyaura, A. Suzuki, Bull. Chem. Soc. Jpn. **65** (1992) 2863
[26] F. Bracher, T. Papke, Phosphorus Sulfur Silicon Relat. Elem., in print
[27] N. Miyaura, M. Ishikawa, A. Suzuki, Tetrahedron Lett. **33** (1992) 2571
[28] J. A. Soderquist, G. Leon, J. C. Colberg, I. Martinez, Tetrahedron Lett. **36** (1995) 3119

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