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Current Trends in the Synthesis of Practically Important Five-Membered Boracarbocycles by Transmetalation of Aluminacarbocycles with Boron Halides †

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Abstract: The data obtained by the authors in the field of chemistry of substituted borolanes and 2,3-dihydro-1*H*-boroles are summarized. The authors developed a selective method for the synthesis of five-membered boracarbocycles via transmetalation of aluminacarbocycles, obtained by the catalytic cycloalumination of unsaturated compounds (terminal olefins or acetylenes) with $AlEt_3$ in the presence of Cp_2ZrCl_2 as a catalyst by boron halides ($BF_3 \cdot Et_2O$, BCl_3, and BBr_3). Some examples of the use of this approach to modify steroid compounds (in particular, to introduce a borolan fragment into them) are described in this review.

Keywords: borolanes; 2,3-dihydro-1*H*-boroles; transmetalation; cycloalumination; boron halides; alkenes; alkynes; Cp_2ZrCl_2; five-membered boracarbocycles

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1. Introduction

There are only a few methods and approaches to synthesize five-membered organoboron compounds. Borolane derivatives were prepared from 1,4-dienes via cyclic hydroboration (Brown reaction) using monochloroborane etherate [1] or isopinocampheylchloroborane etherate [2] and thermal disproportionation of trialkylboranes [3,4]. 2,5-Dihydro-1*H*-borole (borol-3-enes, 1-boracyclopent-3-enes) derivatives were originally prepared by Zweifel [5] from conjugated enynes in a two-step reaction sequence involving the hydroboration and subsequent photocyclization of dienylborane. Herberich [6,7] reported the preparation of 2,3- and 2,5-dihydro-1*H*-boroles via the reaction of the Cl_2BNR_2 substrate with an oligomeric "butadiene-magnesium" reagent. Examples were found where 2,3-dihydroborole systems are readily formed through treatment of dicyclopropylacetylene with the strongly electrophilic borane $B(C_6F_5)_3$ [8].

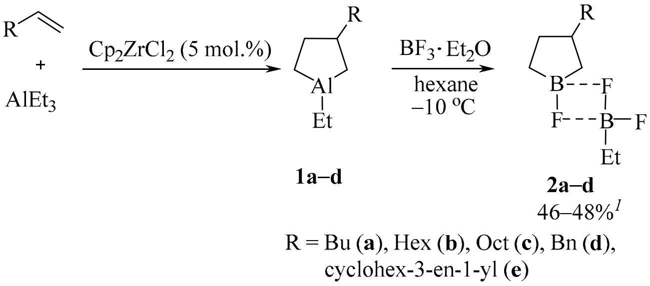
Borolanes and 2,3-dihydroborole are also prepared by transmetalation of cyclic and acyclic organometallic compounds of transition or non-transition metals with various boron derivatives [9,10]. Prior to our studies, organoaluminum compounds were not used to obtain boracarbocycles.

This review summarizes and systematizes the results of the authors' studies on the synthesis and study of the properties of five-membered cyclic organoboron compounds (borolanes and 2,3-dihydro-1*H*-boroles) via transmetalation of cyclic organoaluminum compounds with boron halides.

2. Results and Discussion

To date, we have accumulated significant experience in the development of effective one-pot methods for the synthesis of five-membered boracarbocycles via transmetalation of aluminacarbocycles, obtained by catalytic cycloalumination [11,12] of unsaturated compounds (olefins or acetylenes) with $AlEt_3$ in the presence of Cp_2ZrCl_2 as a catalyst under solvent-free conditions, by boron halides ($BF_3{\cdot}Et_2O$, BCl_3, and BBr_3).

So, in 2012, we developed an efficient one-pot method for the synthesis of 1-fluoro-substituted borolanes **2a–d** through exchange reaction between aluminacyclopentanes **1a–d** and the boron trifluoride–diethyl ether complex [13–15] (Scheme 1). The 1,3-disubstituted borolanes **2a–d** were isolated as molecular complexes with $EtBF_2$.



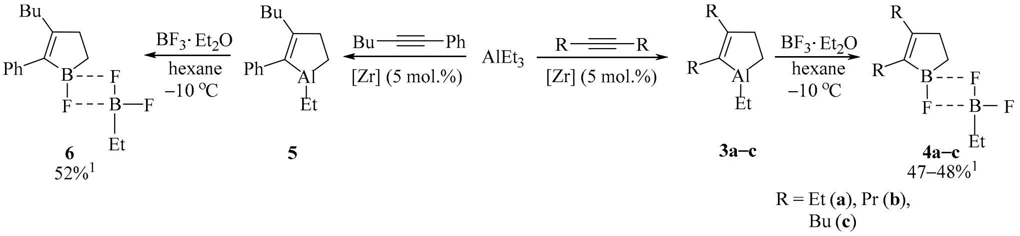
Scheme 1. The synthesis of 1-fluoro-substituted borolanes **2a–d** via transmetalation of aluminacyclopentanes with $BF_3{\cdot}Et_2O$ ([1] Isolated yield after distillation).

$EtBF_2$ is formed as a result of the exchange reaction between $EtAlF_2$ and $BF_3{\cdot}Et_2O$, whereas $EtAlF_2$ is the product of the transmetalation of aluminacyclopentane with $BF_3{\cdot}Et_2O$ (Scheme 2).

$$EtAlF_2 + BF_3{\cdot}Et_2O \longrightarrow EtBF_2 + AlF_3 + Et_2O$$

Scheme 2. The reaction between $EtAlF_2$ and $BF_3{\cdot}Et_2O$.

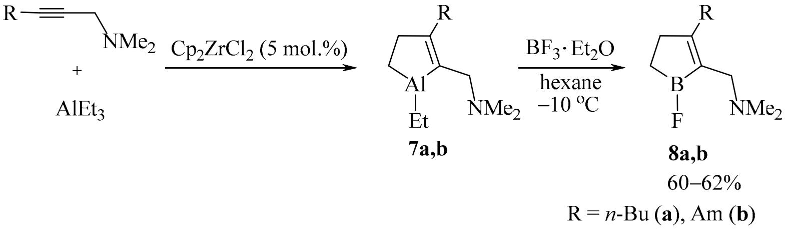
Continuing these works to study the exchange reactions between various aluminacyclanes and boron halides, we developed a one-pot method for the synthesis of unsaturated cyclic organoboron compounds, 2,3-dihydro-1*H*-boroles **4a–c**, by the reaction between 1-ethyl-2,3-dialkylsubstituted aluminacyclopentenes **3a–c**, synthesized by the cycloalumination of disubstituted acetylenes with Et_3Al in the presence of a Cp_2ZrCl_2 as a catalyst [16,17] and $BF_3{\cdot}Et_2O$ [18,19] (Scheme 3).



Scheme 3. The synthesis of 1-fluoro-substituted 2,3-dihydro-1*H*-boroles **4a–c**, **6** via transmetalation of aluminacyclopent-2-enes with $BF_3{\cdot}Et_2O$ ([1] Isolated yield after distillation).

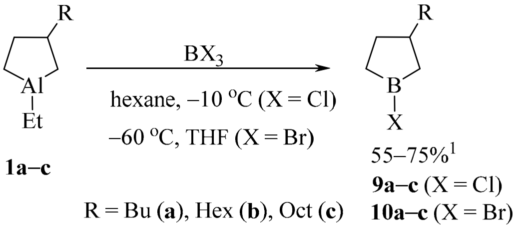
It has been established that aluminacyclopent-2-enes obtained from unsymmetrical acetylenes, for example, butylphenylacetylene, can also be successfully converted into the corresponding substituted 2,3-dihydro-1*H*-boroles. So, 1-ethyl-2-phenyl-3-butylaluminacyclopent-2-ene **5** reacts with $BF_3{\cdot}Et_2O$ to give 4-butyl-2,3-dihydro-5-phenyl-1-fluoro-1*H*-borole **6** in a yield of 52% (Scheme 3). The 2,3-dihydro-1*H*-boroles also form complexes with $EtBF_2$. The yields of borolanes and 2,3-dihydro-1*H*-boroles (Schemes 1 and 3) correspond to the isolated products. However, the monitoring of the transmetalation reaction by ^{1}H, ^{13}C, ^{11}B, ^{27}Al, and ^{19}F NMR spectroscopy showed that aluminacarbocycles were completely transformed into the corresponding boracyclanes. It should be noted that the signals of boron atoms for the obtained borolanes **2a–d** and 2,3-dihydro-1*H*-boroles **4a–c** in the ^{11}B NMR spectra were recorded in a rather low-field region (80–93 ppm).

The aluminacyclopent-2-enes **7a**,**b** [20] with nitrogen-containing substituents can also be successfully transmetalated with $BF_3 \cdot Et_2O$ to the corresponding substituted 2,3-dihydro-1H-boroles **8a**,**b**, which, in contrast to the above 2,3-dialkyl-2,3- dihydro-1H-boroles **4a–c**, were isolated as individual compounds (Scheme 4). The values of δ_B in the ^{11}B NMR spectrum for 2,3-dihydro-1*H*-boroles **8a**,**b** are ~5.2 ppm ($CDCl_3$) and correspond to the region of the tetracoordinated boron atom. Intra- or intermolecular interaction between heteroatoms B and N takes place in a non-polar solvent. There are no signals of $EtBF_2$ in the NMR spectra [18].

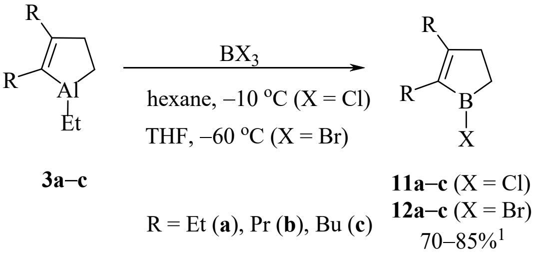


Scheme 4. The synthesis of (3-alkyl-1-fluoro-4,5-dihydro-1*H*-borol-2-yl)- N,N-dimethylmethanamines **8a**,**b**.

The obtained results on the synthesis of boracarbocycles with $BF_3 \cdot Et_2O$ stimulated the studies of B–Al exchange reactions in the series of aluminacyclopentan(en)es with BCl_3 and BBr_3 as the boron regents [21–23]. We found that boron trichloride and tribromide successfully interact with the aluminacyclopentanes **1a–c** and aluminacyclopent-2-enes **3a–c** to form 1-chloro(bromo)-substituted borolanes **9a–c** and **10a–c** and 2,3-dihydro-1*H*-boroles **11a–c** and **12a–c** (Schemes 5 and 6). However, 1-chloro(bromo)-substituted five-membered boracyclanes were isolated individually and do not form a complex with $EtBHal_2$ (Hal = Cl, Br) under the reaction conditions.



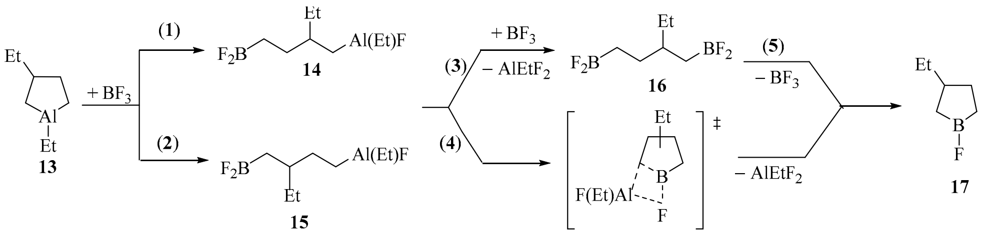
Scheme 5. The synthesis of 1-chloro(bromo)-substituted borolanes **9a–c** and **10a–c** via transmetalation of aluminacyclopentanes with BCl_3 and BBr_3 ([1] Isolated yield after distillation).



Scheme 6. The synthesis of 1-chloro(bromo)-substituted 2,3-dihydro-1*H*-boroles **11a-c** and **12a-c** via transmetalation of aluminacyclopent-2-enes with BCl_3 and BBr_3 ([1] Isolated yield after distillation).

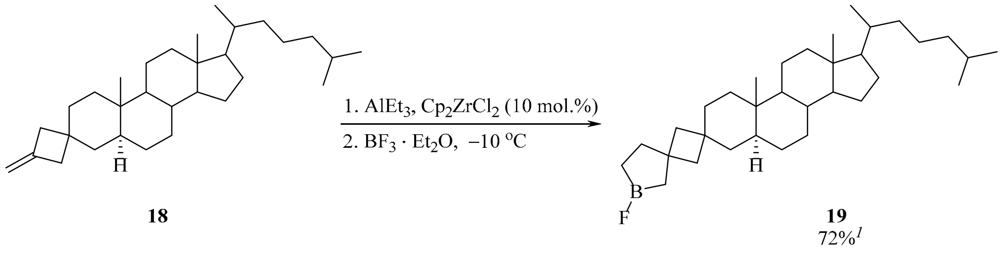
The reaction with BBr_3 requires special conditions: the cooling of the reaction mass to –60 °C followed by the addition of THF. This is due to the fact that 1-bromo-substituted boracarbocycles decompose during thermal distillation, but if THF is added, they form donor–acceptor molecular complexes (**10a–c**)·$(THF)_n$ and (**12a–c**)·$(THF)_n$, which, in the conditions of thermal distillation, stabilize the borolanes **10a–c** (Scheme 5) and 2,3-dihydro-1H-boroles **12a–c** (Scheme 6), preventing decomposition [21,23].

The mechanism of Al−B exchange was studied, taking into account possible reaction routes by the quantum–chemical method PBE/3z (Priroda 6.0) [24–26]. It has been established that acyclic Al,B-adducts **14** and **15** (Scheme 7) are formed with equal probabilities at the first stage, because both reactions (**1**) and (**2**) are characterized by negative Gibbs energies (−9.0 kcal/mol) and similar energy barriers. Further, the target borolane **17** can be formed by two reaction routes: through the intermediate diboron derivative **16** according to the reaction (**3**) or through an alternative route (**4**) as a result of a one-step intramolecular cyclization. Computer simulation taking into account the solvation effect showed that the reactions proceed with a lower barrier. This was confirmed by NMR monitoring of the reaction—^{13}C, and the ^{1}H NMR spectra of the reaction mixture in THF correspond to the cyclic product **17**, while in toluene, only diboron derivatives are formed. Obviously, the diborane derivative obtained in the nonpolar solvent (hexane or toluene) (Scheme 1), is transformed into cyclic borane during thermal distillation. At the same time, borolane was not isolated by distillation from a solution of tetrahydrofuran because of destruction of the cycle.

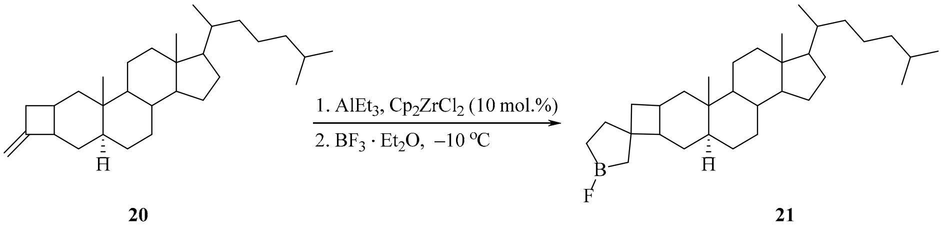


Scheme 7. The transformation of 1,3-diethylalumolane **13** into 1-fluoro-3-ethylborolane **17**.

In 2013, the Cp_2ZrCl_2-catalyzed cycloalumination of cholestane derivatives (3′-methylene-spiro[(5α)-cholestane-3,1′-cyclobutane] **18** and 2′-methylidene-2′,3′-ethano-(5α)-cholestane) **20** with Et_3Al to give spiroalumincarbocycles was performed for the first time. The latter were converted with $BF_3 \cdot Et_2O$ into the corresponding boraspirocarbocycles **19**,**21** without preliminary isolation [27,28] (Schemes 8 and 9).



Scheme 8. The synthesis of borolane **19** based on (3′-methylene-spiro[(5α)-cholestane-3,1′-cyclobutane]. (^{1} Yields determined by weighing the oxidation reaction products, isolated by column chromatography).



20

21
64%^{1}

Scheme 9. The synthesis of borolane **21** based on 2′-methylidene-2′,3′-ethano-(5α)-cholestane (^{1} Yields determined by weighing the oxidation reaction products, isolated by column chromatography).

This method was extended to methylenecyclobutane terpene derivatives (D(+)camphor, (+)-camphene, β-pinene, and L(−) menthol)) to obtain the corresponding boron-containing terpenoids [29].

3. Conclusions

In summary, new effective one-pot methods for the synthesis of borolanes and 2,3-dihydro-1H-boroles by reaction of boron halides with aluminacyclopentanes and aluminacyclopent-2-enes obtained by the Cp$_2$ZrCl$_2$-catalyzed cycloalumination of unsaturated compounds with Et$_3$Al (Dzhemilev reaction) were developed. This method can be used as an effective tool for the functionalization of terpenes, steroids, and their derivatives.

4. Patents

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Conflicts of Interest: The authors declare no conflict of interest.

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