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Published on Web 09/23/2005

A Mild Radical Procedure for the Reduction of *B*-Alkylcatecholboranes to Alkanes

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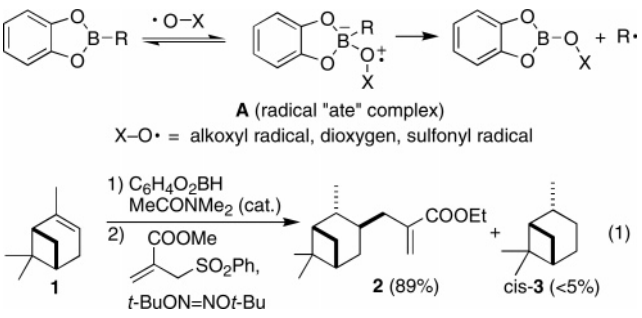
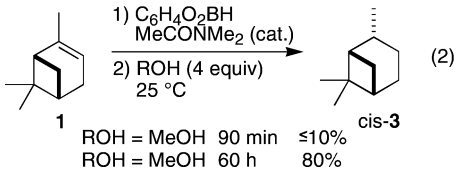
Organoboranes, such as *B*-alkylcatecholborane (2-alkyl-1,2,3-benzodioxaborole), are easily prepared via hydroboration of alkenes.[1−3] Upon oxidative treatment with hydrogen peroxide or other oxidizing agents, alcohols are formed, and the whole process represents an anti-Markovnikov addition of water to alkenes.[4] Reductive treatment of the intermediate alkylboranes leading to alkanes is far less common despite the attractiveness of the procedure for the reduction of double bonds. This transformation is usually achieved by treatment under severe conditions with propionic acid in diglyme at 162 °C,[5−7] alkaline protonolysis,[8,9] and hydrogenolysis at high temperature (190−225 °C).[10,11] We have recently discovered that *B*-alkylcatecholboranes are a very efficient source of alkyl radicals under dioxygen and peroxide initiation (Scheme 1).[12,13] Several chain reactions involving alkoxyl and

Scheme 1

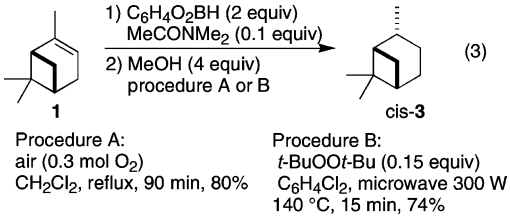


sulfonyl radical intermediates were developed for the formation of carbon−carbon bonds, such as conjugate additions and allylation processes (Scheme 1, eq 1).[14−16] Since radical reactions are particularly mild, we decided to investigate the use of such a process to achieve the reduction of *B*-alkylcatecholboranes. Moreover, during the allylation of α-pinene **1**, depicted in eq 1, we always noticed the formation of a small amount (≤5%) of *cis*-pinane *cis*-**3**.[16] The presence of *cis*-**3** was attributed, without any experimental support, to partial protonation of the intermediate organoborane by the methanol used to deactivate the excess catecholborane. A careful investigation of this process led us to develop a mild method for the reduction of *B*-alkylcatecholboranes. A very unusual use of methanol and related alcohols as reducing agent in a radical process is described.

The reduction of α-pinene **1** to *cis*-pinane *cis*-**3** was used as a model reaction for our initial investigation (eq 2). The hydroboration of **1** is carried out by heating in refluxing dichloromethane with 2 equiv of freshly distilled catecholborane and 10 mol % of *N*,*N*-dimethylacetamide as catalyst.[18] The excess catecholborane was decomposed by addition of MeOH (4 equiv), and the reaction was maintained at room temperature under nitrogen. The formation of pinane **3** was monitored by GC analysis using phenylcyclohexane as an internal standard. After 90 min, *cis*-pinane *cis*-**3** was present in less than 10% yield. The conversion of the organoborane to pinane was slow, and a yield of 80% was obtained after 60 h. Various alcohols were then tested to optimize the reaction conditions. In contrast to our expectation, the acidity of the alcohol did not seem to play an important role in this process. 2-Propanol, *tert*-butyl alcohol, and hexafluoro-2-propanol gave the desired *cis*-**3** in less than 10% yield after 60 h under the conditions described above. Trifluoroethanol and water gave *cis*-**3** in 40 and ≥80% yield, respectively.



However, under very strict exclusion of oxygen (glovebox), the reaction depicted in eq 2 affords only traces (≤5%) of *cis*-**3** after 3 days. Therefore, the role of oxygen was investigated. The reaction is strongly accelerated when air is added slowly to the reaction mixture following the addition of methanol (eq 3). Optimization of the reaction conditions led to the following procedure: hydroboration (2 equiv of CatBH, 10 mol % of $MeCONMe_2$, 5 h reflux in CH_2Cl_2)[18] followed by reduction of the organoborane by adding MeOH (4 equiv) followed by air (0.3 equiv of O_2) over 90 min in refluxing CH_2Cl_2 (procedure A). Under these conditions, a yield of 80% was obtained at the end of the oxygen addition. Similar results were obtained by initiation with di-*tert*-butyl peroxide in dichlorobenzene at 140 °C under microwave irradiation in 15 min (procedure B). Different alcohols were tested: ethanol, 2-propanol, and water gave similar results (GC yield ≥70%). However, *tert*-butyl alcohol and 2-phenylethanol gave the reduced product *cis*-**3** in low yield (23% in both cases).

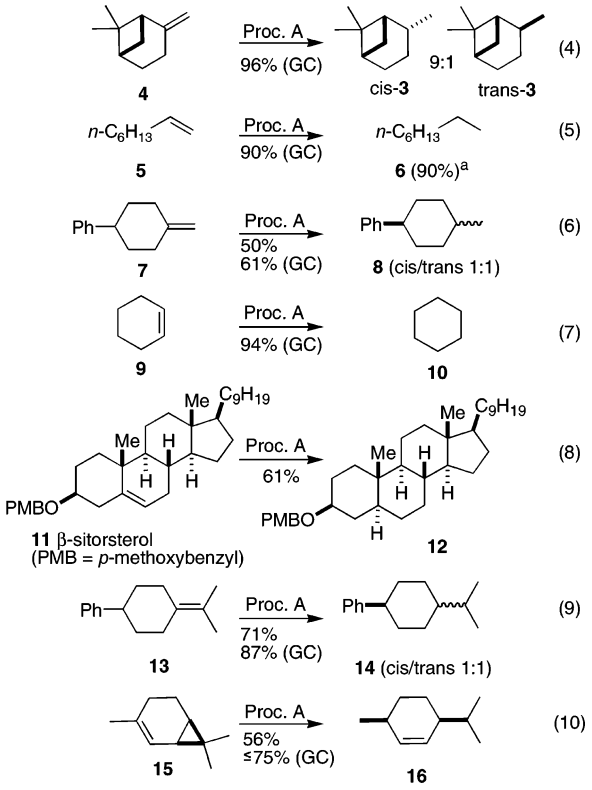


The scope and limitations of the reaction were then investigated for a series of different *B*-alkylcatecholboranes (Scheme 2). Good yields were obtained with primary (eqs 4−6), secondary (eqs 7 and 8), and tertiary (eq 9) alkyl groups. The reduction of 2-carene **15** leads to the monocyclic *cis*-*para*-menth-2-ene **16**, resulting from the ring opening of the cyclopropane ring, demonstrating that a radical intermediate is involved (eq 10).[19]

Reaction of isolated *B*-pinylcatecholborane, prepared by hydroboration of α-pinene and purified by distillation, with methanol (4 equiv) under oxygen initiation affords the reduced product *cis*-**3** in

10.1021/ja055691j CCC: $30.25

Scheme 2. Procedure A: (1) $C_6H_4O_2BH$ (2 equiv), $MeCONMe_2$ (0.1 equiv); (2) MeOH (4 equiv), Air (0.3 mol % of O_2), CH_2Cl_2, Reflux, 90 min

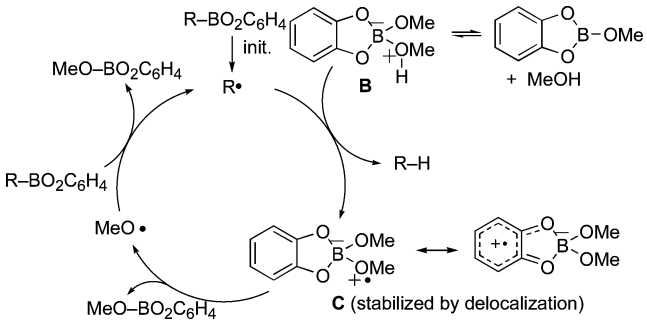


less than 5% yield. However, when a mixture of catecholborane (1 equiv) and MeOH (4 equiv) is added to the pure *B*-pinylcatecholborane, *cis*-**3** is obtained in 43% yield. This demonstrates that the presence of $MeO-BO_2C_6H_4$, resulting from the methanolysis of the excess catecholborane, is an essential component of the reaction.

To investigate further the mechanism of the reaction, we performed deuterium labeling experiments with α-pinene **1**. Reaction in methylene chloride-d_2 initiated by oxygen (procedure A) affords exclusively the nondeuterated pinane *cis*-**3**. Yields and reaction time are similar to those in the reaction in nondeuterated methylene chloride. Reactions with methanol-d_1 (CH_3OD) and -d_4 (CD_3OD) (procedure B) afford the deuterated pinane-d_1, and the reaction becomes very slow (≤17% yield). By using methanol-d_3 (CD_3OH), the nondeuterated *cis*-**3** is obtained in 43% yield (conditions B). These results demonstrate that the transferred hydrogen atom comes from the O−H bond of methanol. Similar results were obtained when the reduction process was run in refluxing methylene chloride using dioxygen as the initiator (procedure A).

A plausible mechanism is depicted in Scheme 3. Reaction of the *B*-alkylcatecholborane with the initiator (oxygen or a *tert*-butoxyl radical) affords the alkyl radical, which is then reduced by **B** resulting from the complexation of MeOH by the Lewis acidic $MeO-BO_2C_6H_4$.[20] The resulting radical **C** is closely related to the radical ate complex **A** (Scheme 1) involved in the formation of alkyl radical from *B*-alkylcatecholborane and is therefore stabilized by delocalization.[21] This radical leads eventually to $MeO-BO_2C_6H_4$ and a methoxyl radical that can react with the alkylcatecholborane to sustain the chain process. This mechanism fits well with the experimental results: (1) the reaction is inhibited by 1,4-cyclohexadiene, presumably due to hydrogen transfer to the methoxyl radical; (2) the deuteration experiment leads to D-incorporation from the O−D bond, the very strong effect on the reaction rate, and

Scheme 3. Mechanistic Proposal



efficiency of the reaction indicates that the hydrogen transfer from the complex **B** to the alkyl radical is a very critical step in the whole process; (3) the inefficiency of the reaction with *tert*-butyl alcohol and 2-phenylethanol can also be explained by rapid fragmentation of the intermediate alkoxyl radicals, leading to methyl and benzyl radicals.[22]

In conclusion, we have developed a method for the reduction of organoboranes with alcohols under mild conditions. This is, to our knowledge, the first radical-mediated reduction of organoboranes. Moreover, the fact that the O−H bond of the alcohol complexed by a Lewis acid is delivering the hydrogen atom is surprising and offers new opportunities for the design of novel tin-free radical reducing agents.

Acknowledgment. We thank the Swiss National Science Foundation (Projects 20-103627 and 20C321-101069) and the University of Bern for financial support, as well as BASF Corporation for the gift of catecholborane.

Supporting Information Available: Detailed experimental procedures and spectroscopic data for new compounds, and further evidence for a radical mechanism based on the reaction of 2-phenylmethylenecyclopropane. This material is available free of charge via the Internet at http://pubs.acs.org.

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JA055691J