Role of catechol in the radical reduction of *B*-alkylcatecholboranes in presence of methanol†

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Mechanistic investigations on the previously reported reduction of *B*-alkylcatecholboranes in the presence of methanol led to the disclosure of a new mechanism involving catechol as a reducing agent. More than just revising the mechanism of this reaction, we disclose here the surprising role of catechol, a chain breaking antioxidant, which becomes a source of hydrogen atoms in an efficient radical chain process.

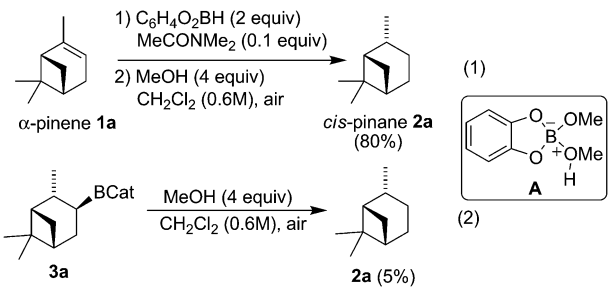
Since the seminal work of H. C. Brown, organoboranes have been widely used in organic synthesis.[1] They are easily obtained *via* hydroboration of alkenes and subsequent oxidation of the resulting alkylborane leads efficiently to the corresponding alcohol.[2] However, reduction of alkylboranes to saturated compounds is far less described. This transformation is usually achieved by treatment under severe conditions with propionic acid in refluxing diglyme,[3] alkaline protonolysis,[4] or hydrogenolysis at high temperature (190–225 °C).[5] Only the selective radical reduction of one alkyl group of a trialkylborane by an alkylthiol has been described to proceed efficiently at room temperature.[6]

We have recently reported a mild procedure for the hydrogenation of alkenes *via* hydroboration with an excess of catecholborane (2 equiv.) followed by treatment with methanol (4 equiv.) in the presence of air as a radical initiator. A typical example, the reduction of α-pinene **1a** to pinane **2a**, is shown in Scheme 1, eqn (1), similar results were obtained with a wide range of primary, secondary and tertiary alkylcatecholboranes.[7] Surprisingly, when the pure organoborane intermediate **3a** was treated with methanol (4 equiv.) under the same reaction conditions, only a very low yield of pinane **2a** (5%) was obtained [eqn (3)]. As a consequence, it was proposed that complex **A** resulting from the complexation of methoxycatecholborane **4** (MeOBCat, generated *in situ* from the excess of catecholborane and methanol) and methanol was the main source of hydrogen atoms in eqn (1). It was hypothesized that the O–H bond of methanol was activated by the complexation with the Lewis acidic MeOBCat. Similar mechanisms were proposed for the reduction of radicals with trialkylborane–water mixtures[8–10] and for the reduction with a titanium–aqua complex.[11]

So far, no direct experimental evidence for the presence of complex **A** in solution has been reported. We report here a detailed investigation of the reaction mechanism for the reduction of *B*-alkylcatecholborane **3** in presence of methanol based on NMR experiments and a new mechanism involving free catechol as reducing agent is proposed.

In order to determine the rate constant of the reduction of the radical by complex **A**, it was necessary to determine the effective concentration of the active species **A** in solution during the reduction process. In 1985, the study of triphenylborane–methanol complexation was reported.[12] The rate of exchange between the complex and free species is fast enough within NMR time scale to give only one weighted average signal. Complexation was able to shift the triphenylborane peak in ^{11}B-NMR from 68 ppm in the absence of methanol to 39 ppm in the presence of 3 equivalents of methanol. Under these conditions, approximately 70% of the triphenylborane was present as a complex.

Similar behavior, *i.e.* a significant upfield shift of the ^{11}B-NMR signal, was expected for the complex between methanol and MeOBCat **4**. Therefore, ^{1}H-NMR and ^{11}B-NMR spectra of MeOBCat **4** in C_6D_6 and in the presence of increasing amounts of methanol (0.5 to 2 equiv.) were recorded (Fig. 1). In the absence of methanol, a single ^{11}B NMR signal at 23.5 ppm was observed (Fig. 1, spectrum a). A very small upfield shift (0.6 ppm) of the ^{11}B-NMR signal was observed when methanol was added to MeOBCat **4**. However, a second signal appeared at 18.8 ppm, increasing in relative intensity with the amount of methanol (Fig. 1, spectra b–d). The signal at 18.8 ppm matches the signal observed for trimethylborate **5** (Fig. 1, spectrum f). This initial



Scheme 1 Alkene hydrogenation *via* hydroboration-radical hydrogen transfer.

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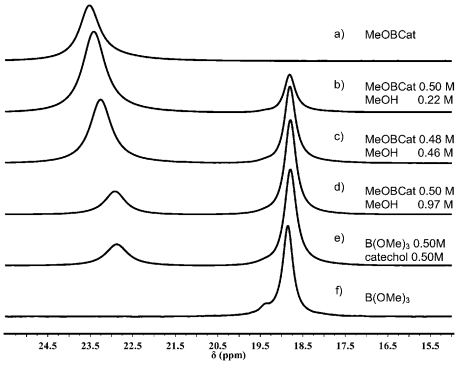
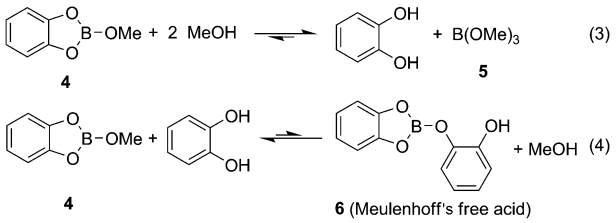
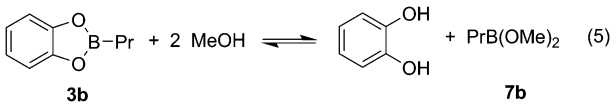


Fig. 1 ^{11}B-NMR of MeOBCat **4** in the presence of methanol.



Scheme 2 Methanolysis of MeOBCat **4**.



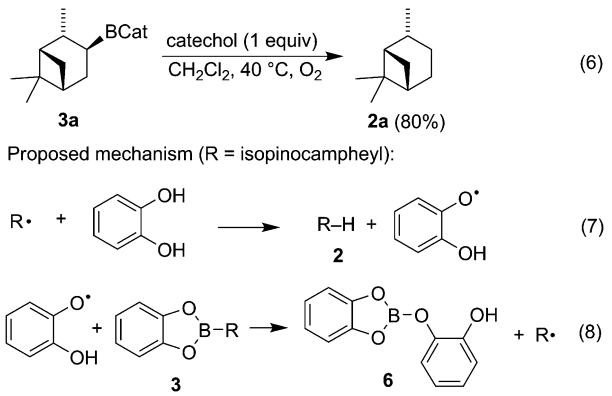
Scheme 3 Methanolysis of PrBCat **3b**.

result indicates that methanolysis of MeOBCat **4** according to eqn (3) takes place rather than formation of complex **A**.

This was further demonstrated by the experiment where $(MeO)_3B$ **5** and catechol were mixed together in benzene leading to the same spectrum as the one obtained by mixing MeOBCat **4** and methanol (Fig. 1, spectrum e). However, a precise interpretation of these results is difficult since both ^{1}H and ^{13}C-NMR spectroscopy show broad aromatic signals indicating that a second fast equilibrium between the remaining MeOBCat **4** and the free catechol is probably taking place according to eqn (4) (Scheme 2). This equilibrium generated the boric ester **6** known as the Meulenhoff's free acid.[13] This could also explain the slight upfield shift observed for the MeOBCat **4** signal in ^{11}B-NMR. Neglecting the formation of **6**, the equilibrium constant for the transesterification of MeOBCat **4** with MeOH [eqn (3)] can be estimated from ^{11}B-NMR integration to be $K_3 = 14\ M^{-1}$. To avoid complications resulting from the reaction of catechol with MeOBCat **4** depicted in eqn (4) (Scheme 2), a similar methanolysis study was performed with *B*-n-propylcatecholborane **3b** (PrBCat).[14] The ^{11}B-NMR spectrum in benzene gives a single signal at 35.8 ppm. Addition of methanol gives rise to a second signal at 31.9 ppm that was attributed to $PrB(OMe)_2$ **7b**. ^{1}H and ^{13}C-NMR spectra gives further evidence for the partial methanolysis of PrBCat **3b** as the spectrum of **3b**/MeOH mixture represents the superposition of those of **3b** and **7b** (see supporting information for copies of spectra†). The absence of a significant modification of chemical shifts in ^{11}B-NMR ($\Delta\delta \leq 0.07$ ppm), ^{13}C-NMR ($\Delta\delta \leq 0.03$ ppm), and ^{1}H-NMR ($\Delta\delta \leq 0.01$ ppm) between pure PrBCat **3b** and **3b** in the presence of variable amounts of methanol indicates that no significant amount of a complex is formed. This result is in accordance with the study of boronic esters transesterification by Brown who reported that no tetracoordinated intermediate could be detected by ^{11}B-NMR.[15] The equilibrium constant for methanolysis of PrBCat **3b** according to eqn (5) (Scheme 3) can estimated to be $K_5 = 0.3\ M^{-1}$. This value indicates clearly that *B*-alkylcatecholborane **3** does not undergo methanolysis to the same extend than MeOBCat **4** (compare eqn (3) and (5)). When *tert*-butanol was used instead of MeOH in the reduction process depicted in eqn (1) (Scheme 1), the reduced product was obtained in very low yield.[7] Interestingly, ^{1}H-NMR spectroscopy of a mixture of PrBCat and *tert*-butanol shows no transesterification, probably due to the bulkiness of the *tert*-butyl group.

All our experimental results (*vide supra*) indicate that boronate complexes such as **A** cannot be the source of hydrogen atoms for the reaction depicted in eqn (1). Therefore, free catechol remains as the most plausible source of hydrogen atoms for this reaction.[16] In order to test this hypothesis, pure *B*-isopinocampheylcatecholborane **3a** was treated with catechol (1 equiv.) using air as an initiator (Scheme 4, eqn (6)). Under these conditions, the pinane **2a** was produced in 80% yield. As expected, no reaction takes place in the absence of air and no reduction is observed in the absence of catechol. The efficiency of the chain process is very remarkable since a substoichiometric amount of oxygen (0.3 equivalent) is sufficient to drive the reaction to completion. The reaction depicted in eqn (6) (Scheme 4) confirms that free catechol is the reducing species.[17] It is able to deliver a hydrogen atom to the alkyl radical (Scheme 4, eqn (7)). This process is followed by a rapid and efficient reaction of the 2-hydroxyphenoxyl radical with the organoborane **3** that propagates the chain process by regenerating the initial alkyl radical and the Meulenhoff's free acid **6** (Scheme 4, eqn (8)). The Meulenhoff's free acid **6** is probably involved in the hydrogen transfer step since reaction in the presence of 0.5 equivalent of catechol affords more than 50% yield of reduced product. Since **6** has been described as a tricoordinated planar boron species in the solid state,[13] its hydrogen donor ability is not expected to exceed that of catechol. It is also reported that two molecules of **6** can liberate free catechol upon formation of $B_2(C_6H_4O_2)_3$.[13] This mechanism is further supported by the study of a 1 : 1 mixture of *B*-propylcatecholborane **3b** and catechol by ^{11}B-NMR. Under an argon atmosphere, only one signal at 35.8 ppm corresponding to **3b** is observed. As soon as a substoichiometric amount of oxygen is allowed to enter the system, a second signal at 23.2 ppm corresponding to the Meulenhoff's free acid **6** appears.[18]

The reduction of *B*-alkylcatecholborane with methanol was shown to be efficient when the boronate ester was prepared *in situ* from an alkene such as α-pinene **1** by using an excess (2 equiv.) of catecholborane and when 4 equivalents of methanol were used. The use of a larger excess of methanol led to a decreased yield. This is best explained by the fact that under these conditions the excess of catecholborane was converted first to MeOBCat and then very rapidly converted to catechol according to eqn (3). The excess of one equivalent of catecholborane used in the hydroboration process consumes



Scheme 4 Reduction of *B*-alkylcatecholborane by catechol.

2.7 equivalents of methanol as 85% of the resulting MeOBcat is methanolysed (estimated from ^{11}B-NMR integration of the reaction mixture). The remaining methanol (1.3 equiv.) is involved in the methanolysis of the *B*-alkylcatecholborane **3** according to eqn (5). Since it is an equilibrated reaction, the concentration of the *B*-alkylcatecholborane **3** remains sufficient to be involved in a radical chain process as only 5% of the PrBCat is methanolysed under these conditions. It is important to note that the *B*-alkyldimethoxyborane **7** is not an efficient source of radicals. The use of larger amount of methanol favors the formation of the unreactive species **7** over **3** and therefore makes the reduction process inefficient (the reduction process gave a very low yield in pure methanol). When pure boronate **3** is used, the reaction is much less efficient (see Scheme 1, eqn (2)). Indeed ^{11}B-NMR analysis of the reaction mixture shows 65% of methanolysis. Therefore both the concentration of catechol and the concentration of the active organoborane **3** are reduced relative to the conditions where the organoboranes was prepared *in situ* with an excess of catecholborane.

In conclusion, based on NMR studies and experimental results, we have revised the mechanism for the reduction of *B*-alkylcatecholboranes by methanol. We disclose here that catechol, a chain breaking antioxidant,[19–21] is acting as a source of hydrogen atom in an efficient radical chain process. This unexpected results is made possible by the fact that aryloxyl radicals undergo a rapid homolytic substitution (SH_2) at the boron atom that prevents the recombination reactions of the aryloxyl radicals.[22,23] These results uncover new opportunities in the quest for reagents to replace tin hydride for radical reduction. Further application of this concept for synthetic purpose is currently under investigation and will be reported in due course.

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