

Radical initiation using borole derivatives

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Abstract

2-Propylbenzo[d][1,3,2]dioxaborole and related derivatives are shown to initiate a range of radical reactions under mild conditions.
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Triethylborane (Et_3B) is a common initiator for a range of radical reactions including halogen-atom transfers,¹ hydroxylations,² deoxygenations,³ conjugate additions,⁴ additions to oximes, imines and aldehydes,⁵ allylations,⁶ and additions of xanthates.⁷ Commonly, in the presence of a hydrogen-atom donor (typically an organotin hydride or silane), it is also used to initiate radical dehalogenations and reductive cyclisations.⁸ All of these reactions are initiated by an $\text{S}_{\text{H}}2$ reaction between Et_3B and O_2 to form $\text{Et}^\bullet$ and $\text{Et}_2\text{BOO}^\bullet$ radicals.⁹ An advantage of this method of initiation, over the use of conventional initiators (such as peroxides and azo compounds), is that radical reactions can be initiated at room temperature, or below, without using specialised photolysis equipment. However, there are problems with using Et_3B . For example, it is spontaneously flammable in air (solutions in hexanes are not pyrophoric), it has a short shelf life, and with it it can be difficult to achieve reproducible results.¹⁰ The problems associated with using Et_3B have limited its use, particularly in industry, and this led us to investigate the use of alternative boranes as radical initiators, particularly, 2-alkylbenzo[d][1,3,2]dioxaboroles.

Renaud and co-workers have utilised the in situ formation of 2-alkylbenzo[d][1,3,2]dioxaboroles as a source of alkyl radicals.¹¹ The benzodioxaboroles, formed in hydroboration reactions of alkenes with catecholborane, react

with oxygen to give alkyl radicals that were shown to undergo conjugate addition to, for example, α,β -unsaturated alkenes. The greater stability and easier handling of 2-alkyl-1,3,2-benzodioxaboroles, compared to Et_3B , suggested that these reagents could find widespread application as radical initiators for a range of reactions.

Our preliminary studies concentrated on comparing the effectiveness of different initiators (0.2 equiv) to promote the reduction of 2-bromoacetophenone (**1**) (1 equiv) using Bu_3SnH (1.1 equiv) in cyclohexane (Fig. 1 and Table 1). Reduction of **1** using AIBN and heating, or Et_3B at rt, gave quantitative yields of acetophenone (**2**) (entries 1 and 2). Other borane initiators, such as **3** and **4**,¹² were equally effective (entries 3 and 4). Borolanes **5** and **6**, and borole **7**, were prepared by hydroboration reactions [catalysed by $(\text{Ph}_3\text{P})_3\text{RhCl}$]¹³ and they were used immediately, without purification, to initiate the quantitative reduction of **1** (entries 5–7).¹⁴ Finally, commercially available 2-propylbenzo[d][1,3,2]dioxaborole **8** (known hereafter as PBD), was also shown to efficiently reduce **1** using Bu_3SnH or $(\text{Me}_3\text{Si})_3\text{SiH}$ (entry 8).

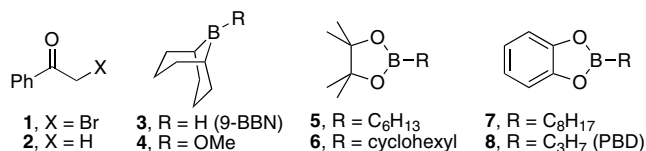


Fig. 1.

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Table 1
Reduction of 2-bromoacetophenone (**1**)

Entry	Initiator	Conditions ^a	Yield of 2 (%)
1	AIBN	Reflux, 24 h, N ₂	99
2	Et ₃ B	rt, 2 h, air	99
3	3	rt, 24 h, N ₂	99
4	4	rt, 24 h, air	99
5	5 ^b	rt, 24 h, air	99
6	6 ^b	rt, 24 h, air	99
7	7 ^b	rt, 24 h, air	99
8	8	rt, 24 h, air	99 ^c (99) ^d

^a Using Bu₃SnH in cyclohexane; for entries 1 and 3, cyclohexane was degassed.

^b Freshly prepared (unpurified) borolane **5–6** or borole **7** was used.

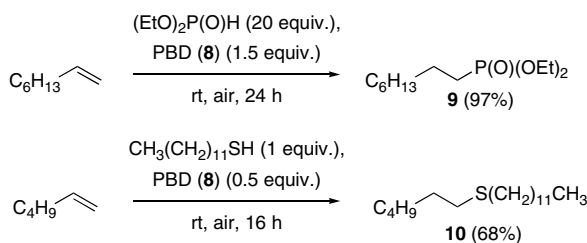
^c A quantitative yield of **2** was also observed after 2 h at rt in cyclohexane, and after 2 h at –78 °C in THF.

^d Using (Me₃Si)₃SiH (1.1 equiv) in place of Bu₃SnH.

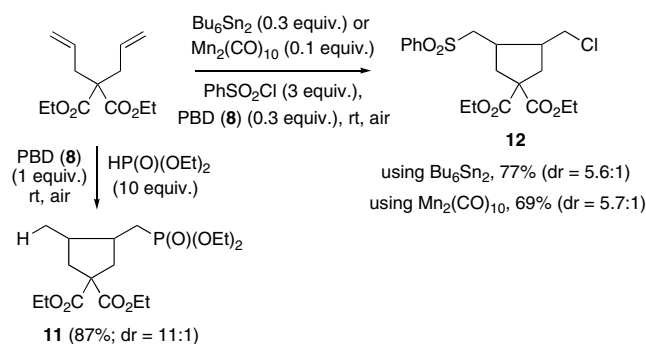
The successful reduction of **1**, using a range of boron-based initiators, led us to probe the use of PBD (**8**),¹⁵ as an initiator for a variety of alternative radical reactions. For example, reduction of neat 10-bromo-1-decene using PBD (0.2 equiv) and Bu₃SnH (1.1 equiv) at rt gave 1-decene in 75% yield. Reduction of xanthates is also possible via the chemoselective reaction of PBD (0.1 equiv) with Bu₃SnH (1 equiv) and 4-BrC₆H₄CH₂S(C=S)OMe (1 equiv) (neat, at rt) to give 4-BrC₆H₄CH₃ in 83% yield after 24 h.

Radical addition of diethyl phosphite to 1-octene proceeded smoothly in the presence of PBD to give phosphonate **9** in 97% yield (Scheme 1). When the same reaction was carried out in cyclohexane (rather than neat), **9** was isolated in a lower yield of 73%. PBD can also initiate the addition of 1-dodecanethiol to 1-hexene, at rt, to give sulfide **10**.

Reaction of diethyl phosphite with diethyl diallylmalonate in an addition–cyclisation reaction, to efficiently form phosphonate **11** (as the cis-diastereoisomer predominantly), was initiated using PBD (Scheme 2). Similarly, PBD initiated the atom-transfer radical cyclisation reaction between diethyl diallylmalonate and benzenesulfonyl chloride, in the presence of hexabutylditin (Bu₆Sn₂) or dimanganese decacarbonyl [Mn₂(CO)₁₀], to give sulfone **12**. In the absence of PBD, or in the absence of Bu₆Sn₂ or Mn₂(CO)₁₀, only starting materials were recovered. Normally, these types of reaction are initiated (at rt) by photolysis, which breaks the Sn–Sn bond in Bu₆Sn₂, or the Mn–Mn bond in Mn₂(CO)₁₀.



Scheme 1. Addition of diethyl phosphite and 1-dodecanethiol to a terminal C=C bond.



Scheme 2. Radical addition–cyclisation reactions of diethyl diallylmalonate (all reactions were carried out over 16 h).

Reductive radical cyclisation of dichloroacetals **13** and **14**, prepared using a reported procedure,¹⁶ can also be initiated using PBD (Fig. 2). For example, reaction of **13** with PBD (1 equiv) and Bu₃SnH (1.1 equiv) in air, at rt, for 18 h gave tetrahydrofuran **15** in 31% yield (as a 4.7:2.5:1 mixture of inseparable isomers, from the ¹H NMR spectrum). Under similar conditions, dichloroacetal **14** gave tetrahydrofuran **16** in 23% yield (as a 9:1.3:1:1 mixture of inseparable isomers).¹⁷ Competitive simple reduction is also observed under these conditions, for example, the reaction of **14** also gave chloroacetal **17** in 76% yield.

Polymerisation of some alkenes can also be promoted using PBD.¹⁸ For example, reaction of methyl methacrylate (10 equiv) with PBD (1 equiv) in toluene at rt in the presence of air, after 24 h, gave poly(methyl methacrylate) in 92% yield (*M*_n = 11,576; PDI = 1.5).¹⁹ Alternatively, reaction of *N*-phenylmaleimide (10 equiv) with PBD (1 equiv) in dichloromethane at rt in the presence of air, after 2 h, gave poly(*N*-phenylmaleimide) in 59% yield (*M*_n = 6362; PDI = 3.1).²⁰ In comparison with Et₃B, it was found that polymerisations promoted by PBD generally gave more reproducible results.

We have also investigated the in situ generation of borole initiators, other than PBD (**8**), and their use in sequential radical reduction/hydroboration–oxidation sequences. For example, reaction of 10-bromo-1-decene (**18**) (1 equiv) with catecholborane (**19**) (1.2 equiv)/CIRh(PPh₃)₃ (5 mol %) gave crude borole **20**, which was used to initiate the reduction of 10-bromo-1-decene (**18**) (5 equiv) by (Me₃Si)₃SiH (5.5 equiv). The crude product was then reacted immediately with further catecholborane (**19**) (5.5 equiv)/CIRh(PPh₃)₃ (5 mol %) followed by H₂O₂/HO[–] to produce 1-decanol (**21**) in 66% yield (the product yield is calculated based on using 6 equiv of **18**) (Scheme 3).

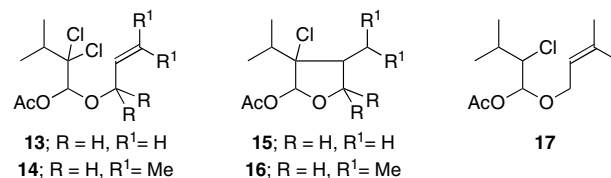
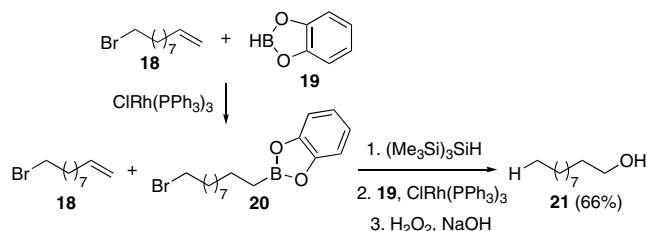


Fig. 2.



Scheme 3. Radical reduction of **18** initiated by borole **20**, followed by sequential hydroboration and oxidation to give 1-decanol (**21**).

In summary, PBD (**8**) and related derivatives are shown to initiate radical reactions under mild conditions. The mechanism of initiation is likely to involve cleavage of the C–B bond in **8**, on reaction with O_2 , to give a propyl radical. In comparison to Et_3B , PBD and related compounds are easier to handle and they can give more reproducible results. The facile preparation of boroles, by hydroboration of alkenes, means that this family of compounds could find wide application as radical initiators.

Acknowledgement

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- PBD (**8**) can be used to polymerise other alkene monomers, at rt, including butyl acrylate, methyl acrylate, methacrylic acid and acrylamide. Parsons, A. F.; Sharpe, D. J.; Taylor, P. unpublished results.