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Radical initiation using borole derivatives

Isabella Montgomery [a], Andrew F. Parsons [a,*], Franco Ghelfi [b], Fabrizio Roncaglia [b]

[a] Department of Chemistry, University of York, Heslington, York, YO10 5DD, UK
[b] Dipartimento di Chimica, Università degli Studi di Modena e Reggio Emilia, via Campi 183, 41100 Modena, Italy

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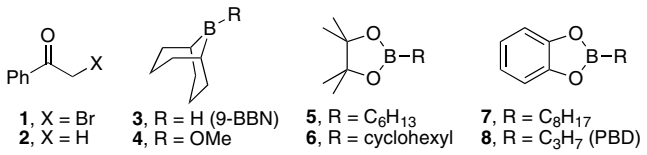
Abstract

2-Propylbenzo[*d*][1,3,2]dioxaborole and related derivatives are shown to initiate a range of radical reactions under mild conditions.

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 S_H2 reaction between Et_3B and O_2 to form $Et^{\cdot}$ and $Et_2BOO^{\cdot}$ 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 $(Ph_3P)_3RhCl$][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 $(Me_3Si)_3SiH$ (entry 8).



1, X = Br
2, X = H
3, R = H (9-BBN)
4, R = OMe
5, R = C_6H_{13}
6, R = cyclohexyl
7, R = C_8H_{17}
8, R = C_3H_7 (PBD)

Fig. 1.

* Corresponding author. Tel.: +44 1904 432608; fax: +44 1904 432516.
E-mail address: afp2@york.ac.uk (A.F. Parsons).

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

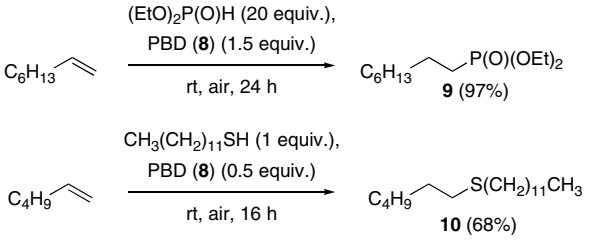
Entry	Initiator	Conditions[a]	Yield of **2** (%)
1	AIBN	Reflux, 24 h, N_2	99
2	Et_3B	rt, 2 h, air	99
3	**3**	rt, 24 h, N_2	99
4	**4**	rt, 24 h, air	99
5	**5**[b]	rt, 24 h, air	99
6	**6**[b]	rt, 24 h, air	99
7	**7**[b]	rt, 24 h, air	99
8	**8**	rt, 24 h, air	99[c] (99)[d]

[a] Using Bu_3SnH 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 $(Me_3Si)_3SiH$ (1.1 equiv) in place of Bu_3SnH.

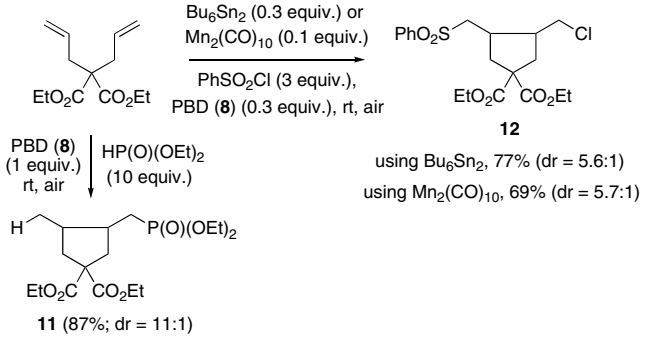
The successful reduction of **1**, using a range of boron-based initiators, led us to probe the use of PBD (**8**),[15] as an initiator for a variety of alternative radical reactions. For example, reduction of neat 10-bromo-1-decene using PBD (0.2 equiv) and Bu_3SnH (1.1 equiv) at rt gave 1-decene in 75% yield. Reduction of xanthates is also possible via the chemoselective reaction of PBD (0.1 equiv) with Bu_3SnH (1 equiv) and 4-$BrC_6H_4CH_2S(C{=}S)OMe$ (1 equiv) (neat, at rt) to give 4-$BrC_6H_4CH_3$ 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 (Bu_6Sn_2) or dimanganese decacarbonyl [$Mn_2(CO)_{10}$], to give sulfone **12**. In the absence of PBD, or in the absence of Bu_6Sn_2 or $Mn_2(CO)_{10}$, only starting materials were recovered. Normally, these types of reaction are initiated (at rt) by photolysis, which breaks the Sn–Sn bond in Bu_6Sn_2, or the Mn–Mn bond in $Mn_2(CO)_{10}$.



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 Bu_3SnH (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 Et_3B, 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)/$ClRh(PPh_3)_3$ (5 mol %) gave crude borole **20**, which was used to initiate the reduction of 10-bromo-1-decene (**18**) (5 equiv) by $(Me_3Si)_3SiH$ (5.5 equiv). The crude product was then reacted immediately with further catecholborane (**19**) (5.5 equiv)/$ClRh(PPh_3)_3$ (5 mol %) followed by H_2O_2/HO^- to produce 1-decanol (**21**) in 66% yield (the product yield is calculated based on using 6 equiv of **18**) (Scheme 3).

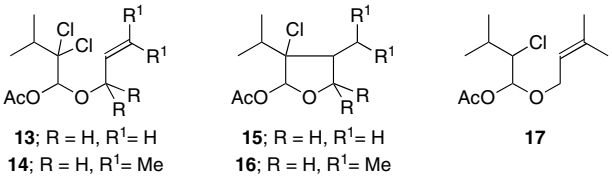
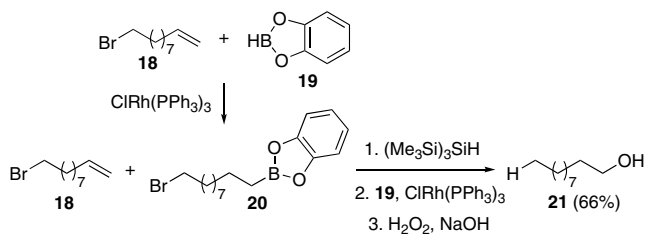


Fig. 2.



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 various 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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14. Cyclohexene (0.05 ml, 0.49 mmol, 0.2 equiv) was stirred with Wilkinson's catalyst (0.005 g, 5 mol %), under N_2, then catecholborane (0.58 ml, 1 M in THF, 0.58 mmol, 0.24 equiv) was added dropwise at 0 °C. The mixture was then allowed to warm to rt and stirred. After 4 h, $HSnBu_3$ (0.76 ml, 2.82 mmol, 1.1 equiv) and bromoacetophenone (**1**) (0.50 g, 2.50 mmol, 1 equiv) were added and the reaction stirred overnight in air. Purification by column chromatography (KF on silica; petrol–EtOAc, 1:1) gave acetophenone (0.39 g, 99%) as a colourless oil. (Catechol byproducts may be removed from the organic product, prior to chromatography, by washing a solution of the crude product in EtOAc with 1 M NaOH).
15. PBD (**8**) is more stable to oxidation in air than Et_3B. After exposure to air for 72 h, the ^1H NMR spectrum indicated mainly unreacted PBD.
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19. The average molecular mass (M_n) and polydispersity (PDI) of polymer samples were obtained using GPC, on a system equipped with a guard column and two Shodex columns (KF-802.5 and KF-803), with a Waters 2410 differential refractive index detector using THF (containing 1% toluene as a marker) at 0.7 ml min^{-1} as eluant. M_n was calculated against nine narrow PMMA standards in the range 5.59×10^5 to 960 g mol^{-1}.
20. 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.