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A flexible access to highly functionalised boronates

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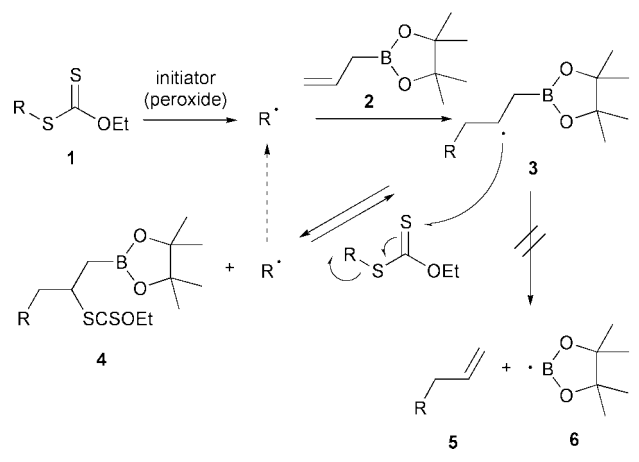
The radical addition of various xanthates to allyl or vinyl boronates occurs smoothly in the presence of a small amount of lauroyl peroxide as initiator to give good yields of usefully functionalised boronates.

The emergence of the poweful palladium induced coupling of boronates with halides, the Suzuki–Miyaura reaction, has caused a renewed interest in the chemistry of boronic acid derivatives.[1] Access to boronates has so far relied heavily on ionic and organometallic processes, with radical reactions playing only a very minor part.[2] The Kharasch addition of halides to vinyl boronates was reported by Matteson some years ago and has been used occasionally since.[3] In one, more recent work, simple radicals generated using stannane chemistry or through the Barton decarboxylation were found to add to vinyl boronates.[4] Ring-closures of radicals α-to the boron atom have also been described.[5] Recent theoretical studies seem to indicate that boronates have a much lower stabilising influence on an adjacent radical, in comparison to boron groups with less donating substituents.[6] In the present communication, we describe a flexible approach to functionalised boronates by application of the xanthate transfer radical addition[7] to both allyl and vinyl boronates.

The radical addition sequence is summarised in Scheme 1 for the case of allyl boronate **2**. Thus, radical **R**·, generated from xanthate **1** by the action of the initiator, undergoes addition to the least hindered end of the terminal olefin to give a new radical **3**, which then engages in a reversible addition–fragmentation process leading to adduct **4** with the concomitant regeneration of radical **R**· to propagate the chain. Addition to the unactivated olefinic bond is possible because **R**· is *not* competitively consumed by reaction with xanthate **1** (this reaction is both reversible and degenerate) and its effective lifetime in the medium is therefore significantly increased. Fragmentation of intermediate adduct radical **3** to give olefin **5** and high energy boryl radical **6** did not seem likely in the light of a recent ESR study of radicals adjacent to boronates.[6]

Indeed, when a small amount of lauroyl peroxide was added portion-wise to a refluxing, concentrated solution of xanthate **1a** (1 M) and a 1.5 to 2-fold excess of allyl boronate **2** in 1,2-dichloroethane, a smooth reaction occured to produce adduct **4a** in high yield (Table 1).† The same transformation could be accomplished with a number of other xanthates containing various functional groups, including ketones, esters, nitriles, and even heterocyclic rings, as shown by the varied examples compiled in the Table 1. The yields have not been optimised but nevertheless are generally quite good.

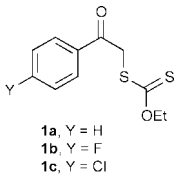
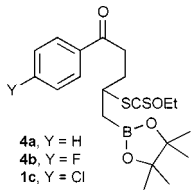
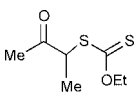
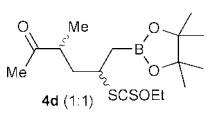
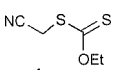
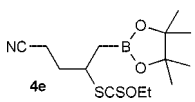
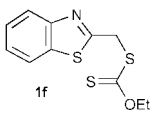
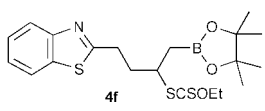
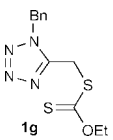
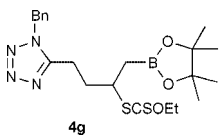


Scheme 1

The xanthate group in the adduct can be efficiently reduced off either by treatment with a stoichiometric amount of lauroyl peroxide in isopropanol,[8] as illustrated by the conversion of **4e** into **7e**, or by using the more traditional tributyltin hydride as in the reduction of **4a** into **7a** (Scheme 2). The former, tin-free procedure is more convenient for large scale work or for producing samples destined for biological testing. The presence of the xanthate group can alternatively be exploited to create another carbon–carbon bond, for example through a ring closure onto an aromatic ring.[9] For instance, addition over a period of one hour of a stoichiometric quantity of lauroyl peroxide to a refluxing solution of adducts **4a** or **4b** in chlorobenzene resulted in the formation of tetralones **8a** and **8b** in 35 and 42% yield respectively.

Finally, by performing the first radical addition on a vinyl boronate such as **9**, the relative position of the various functions present in the initial xanthate with respect to the boronate group can be easily and conveniently modified. The synthesis of compounds **10a** and **10b** (Scheme 3) provides two examples where the xanthate and the boronate groups are now in a geminal disposition.

Table 1 Synthesis of boronates **4**

Xanthate **1**	Boronate **4**	Yield (%)
 **1a**, Y = H **1b**, Y = F **1c**, Y = Cl	 **4a**, Y = H **4b**, Y = F **1c**, Y = Cl	**4a** (94) **4b** (78) **4c** (78)
 **1d**	 **4d** (1:1)	(63)
 **1e**	 **4e**	(85)
 **1f**	 **4f**	(68)
 **1g**	 **4g**	(70)

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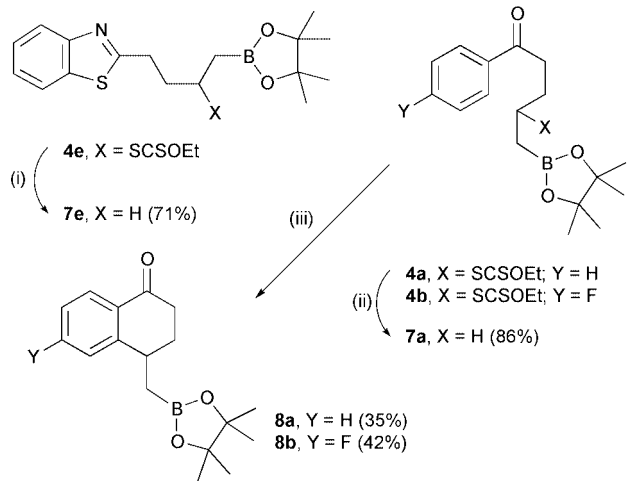
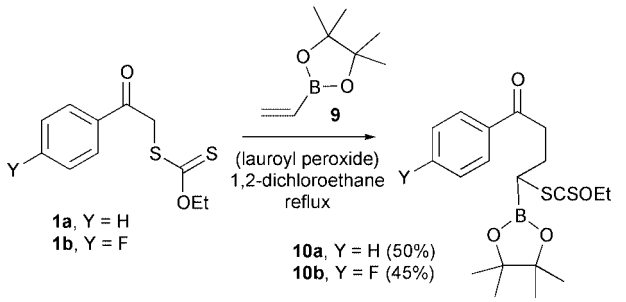


Scheme 2 *Reagents*: (i) lauroyl peroxide (100–110 mol%) propan-2-ol, reflux; (ii) Bu_3SnH, toluene, reflux; (iii) lauroyl peroxide (100–110 mol%), chlorobenzene, reflux.



Scheme 3

The present approach to boronates is simple, yet efficient and flexible. A broad variety of densely functionalised, otherwise inaccessible boronates can be rapidly prepared using cheap and readily available starting materials and reagents.

Notes and references

† *General procedure for the radical addition to allyl and vinyl boronates* **2** *and* **9**. A solution of xanthate **1** (1 mmol) and ally or vinyl boronate **2** or **9** (1.5 mmol) in 1,2-dichloroethane (*ca.* 1 mL) was heated to reflux for 15 min. Lauroyl peroxide (10 mmol%) was then added every 1 h until almost complete consumption of the xanthate. The solvent was removed under reduced pressure and the residue purified by chromatography on silica to give the corresponding adduct **4** or **10**.

Representative spectral and analytical data. (**4a**): ^{1}H NMR (300 MHz, $CDCl_3$): 7.95 (d, J = 6.6 Hz, 2H, H arom), 7.52 (m, 1H, H arom), 7.45 (m, 2H, H arom), 4.62 (m, 2H, OCH_2CH_3), 4.03 (m, 1H, CHS), 3.13 (m, 2H, CH_2CH_2), 2.27–2.10 (m, 2H, CH_2CH_2), 1.39 (t, J = 7.2 Hz, 3H, OCH_2CH_3), 1.37 (d, J = 8.1 Hz, 2H, CH_2B), 1.24 (12H, $4CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$): 214.3, 199.4, 136.9, 133.1, 128.6, 128.2, 83.7, 69.7, 47.5, 36.2, 30.7, 24.9, 13.8. IR (cm^{-1}) ν: 1686 (C=O). Anal. Calc. for $C_{20}H_{29}BO_4S_2$: C, 58.82; H, 7.16. Found: C, 58.85, H, 7.16%.

(**4e**): ^{1}H NMR (300 MHz, $CDCl_3$): 4.67 (q, J = 7.2 Hz, 2H, OCH_2CH_3), 3.99 (m, 1H, CHS), 2.18 (t, J = 7.6 Hz, 2H, $NCCH_2$), 2.12 (m, 2H, $NCCH_2CH_2$), 1.43 (t, J = 7.2 Hz, 3H, OCH_2CH_3), 1.32 (d, J = 7.5 Hz, 2H, CH_2B), 1.25 (bs, 12H, $4CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$): 188.0, 119.4, 83.9, 70.1, 46.4, 32.2, 24.8, 15.1, 13.8. IR (cm^{-1}) ν: 2247. Anal. Calc. for $C_{14}H_{24}BNO_3S_2$: C, 51.07; H, 7.35. Found: C, 51.33, H, 7.47%.

(**10b**): ^{1}H NMR (300 MHz, $CDCl_3$): 7.95-8.10 (m, 2H, H arom), 7.1–7.25 (m, 2H, H arom), 4.55–4.70 (3H, OCH_2CH_3, CHS), 3.18, (t, J = 6.0 Hz, 2H, CH_2CH_2), 2.15–2.37 (m, 2H, CH_2CH_2), 1.4 (t, J = 7.5 Hz, 3H, OCH_2CH_3), 1.28 (bs, 12H, $4CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$): 199.5, 179.3, 136.9, 133.1, 128.6, 128.1, 84.4, 70.13, 37.3, 29.6, 24.9, 14.18. IR (cm^{-1}) ν: 1684, 1598, 1226, 1050. Anal. Calc. for $C_{19}H_{26}BFO_4S_2$: C, 55.34; H, 6.36. Found: C, 55.83, H, 6.07.

(**7e**) A solution of xanthate adduct **4e** (0.23 mmol) in propan-2-ol (1 mL) was heated to reflux for 15 min. Lauroyl peroxide (10 mol%) was then added every 1 h until almost complete consumption of the xanthate (100–110 mol%). The solvent was removed under reduced pressure and the product isolated by chromatography over silica gel with heptane–ethyl acetate (9 : 1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.97 (d, J = 7.2 Hz, 1H, H arom), 7.82 (d, J = 8.1 Hz, 1H, H arom), 7.47 (m, 1H, H arom), 7.33 (m, 1H, H arom), 3.12 (t, J = 7.5 Hz, 2H, CH_2), 1.80 (m, 2H, CH_2), 1.63 (m, 2H, BCH_2), 1.26 (s, 12H, CH_3) 0.90 (m, 2H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): 179.0,172.7, 153.0, 125.8, 124.6, 122.4, 121.4, 83.0, 34.1, 31.9, 29.6, 24.8. Anal. Calc. for $C_{17}H_{24}BNO_2S$: C, 64.36; H, 7.63. Found: C, 64.35, H, 8.21%.

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