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HIGH YIELD PREPARATION OF BORONIC ESTERS OF 1,2-DIOLS WITH LITHIUM TRIALKYLBOROHYDRIDES

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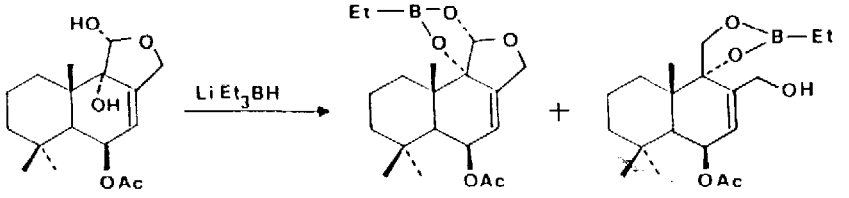
Abstract - *Cyclic Boronic esters of 1,2-diols are easily prepared by reaction of 1,2-glycols with lithium trialkylborohydrides.*

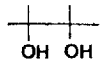
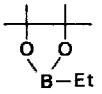
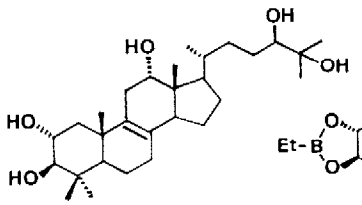
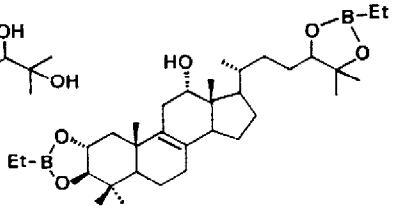
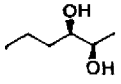
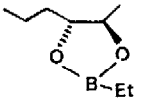
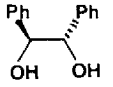
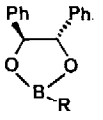
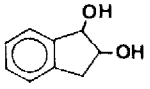
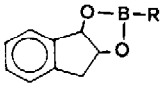
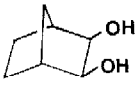
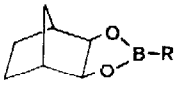
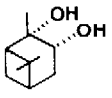
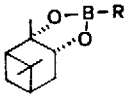
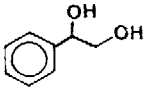
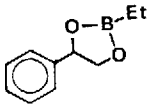
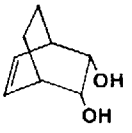
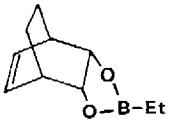
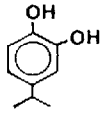
Alkylboronic esters have found extensive applications in organic synthesis in the last decade. The utility of these compounds in C-C, C-O, C-N bonds forming reactions, involving migration of organic groups from boron to carbon, oxygen or nitrogen, has been firmly established.[1] Recently chiral boronic esters have been extensively used in the synthesis of chiral compounds with very high optical purities,[1f-1,2] and in the preparation of a new class of asymmetric reducing agents.[3] Finally boronic esters are useful protecting groups, mainly in carbohydrate chemistry,[4] and as derivatizing agents for difunctional compounds for GC and GC-MS analysis.[5] Although several methods are available for their preparation,[1d,6] the yields are not always satisfactory.[7] In this paper we disclose a new reaction of lithium trialkylborohydrides with 1,2-diols which allows the easy preparation of alkylboronates.

In the course of an ongoing synthetic project, we planned to reduce compound **1** with lithium triethylborohydride, a very well known powerful and selective reducing agent in organic synthesis.[8] We assumed that the cyclic acetal was in equilibrium with the open hydroxy-aldehyde function, allowing the carbonyl group to be easily reduced.



1 **2** **3**

Rather unexpectedly the reaction afforded the two cyclic ethylboronates **2** and **3** (6:1) in good combined yield (80%). Thus it appeared that lithium triethylborohydride could be used not only for its reducing properties, but also as a reagent for the protection of 1,2-diols. Indeed we found that this reaction is general, allowing the preparation of ethylboronic esters of cyclic and acyclic 1,2-diols (Table, entries 1-9) in high to very high yields. To extend the

ENTRY	STARTING COMPOUND	ALKYLBORONATE [a]	YIELD [b]
1			75
2			73
3			70
4			**4** a) R = Et 96 b) R = $CH(CH_3)CH_2CH_3$ 82 c) R = $CH(CH_3)CH(CH_3)_2$ 80 d) R = $CH_2CH_2CH_2CH_3$
5			**5** a) R = Et 78 b) R = $CH(CH_3)CH_2CH_3$ 73
6			**6** a) R = Et 80 b) R = $CH(CH_3)CH_2CH_3$ 77 c) R = $CH(CH_3)CH(CH_3)_2$ 75
7			**7** a) R = Et 85 b) R = $CH(CH_3)CH(CH_3)_2$ 93
8			80
9			98
10		—	

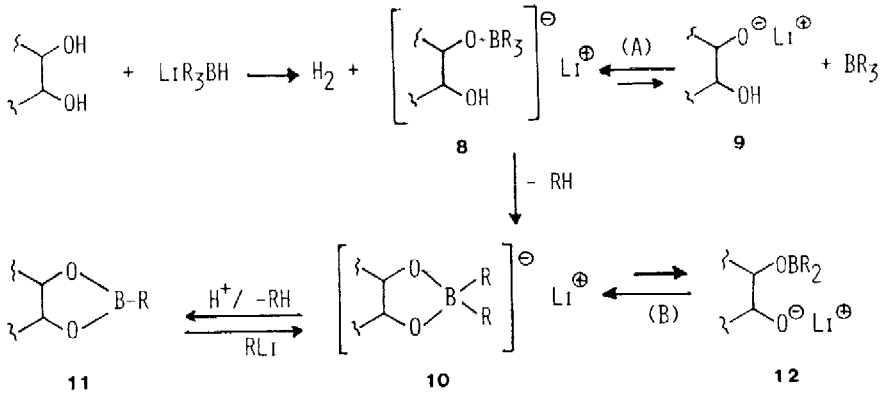
a) Alkylboronates were fully characterized by their IR,NMR,EIMS and GCMS spectra.

b) Yields refer to isolated,analitically pure (TLC and GC) compounds.

application of this method, we tested the reaction of some representative diols with other lithium trialkylborohydrides. As anticipated, sec-butylboronates (**4b**, **5b**, **6b**) and 2-(3-methyl)butylboronates (**4c**, **6c**, **7b**) were smoothly obtained, by using lithium tri-sec-butylborohydride (L-Selectride ®) or lithium trisiamylborohydride (LS - Selectride ®), respectively.

Representative procedure: to a stirred THF solution (2,5 ml) of pinanediol (40 mg, 0,235 mmol), cooled to 0°C under an inert atmosphere, was added via a syringe a 1M THF solution of Lithium triethylborohydride (259 μl, 0.259 mmol).The reaction mixture was stirred at 0°C for 5 min, then at room temperature for 1h and quenched with H_2O. After an additional stirring for 30 min at room temperature volatiles were removed under reduced pressure and the residue was taken up in CH_2Cl_2 and filtered through a Celite-$MgSO_4$ pad. Removal of the solvent left the chromatographically pure ethylboronate (42 mg). In the case of the alkylboronates of entries 1 and 8 the crude residue was purified on a short silica gel column. Elution with hexane-Et_2O (7:1) removed minor amounts of polar unidentified compounds.

The factors which affect the successful outcome of the reaction seem to be the formation and the stability of the lithium "ate" complexes **8** and **10**, and the selective cleavage, by protonation, of the B-C bonds, instead of the B-O bonds of these salts.



Interestingly, no boronate ester could be obtained by reacting catechols (e.g., Table entry 10) with lithium trialkylborohydrides. This can be attributed to the fact that, though phenols evolved hydrogen rapidly and quantitatively, the corresponding lithium salts produced did not coordinate with the trialkylborane,[8a] i.e., with phenols, equilibrium A favours the salt **9** completely. The complex **10** is in equilibrium with the alcoholate **12**, although the equilibrium B favours the salt **10**.[9] Moreover, when the alkoxy groups of the borate species **10** are derived from a 1,2-diol, the alkylboronate **11**, instead of the borinic ester **12**, is formed selectively on destruction of the complex. The above mechanism was supported by the following results:

a) a mixture of boronates **4a** and **4d** was obtained, almost quantitatively, when BuLi (1 eq) was added to a THF solution of the boronate **4a**, followed by addition of H_2O.

b) when, in the above experiment, benzophenone (1 eq) was added to the reaction mixture, before quenching with H_2O, no formation of alkyldiphenylcarbinol could be detected.

c) analogously, no ethyldiphenylcarbinol was obtained when benzophenone (1 eq) was added to the reaction mixture of 1,2-diphenyl-1,2-ethanediol with lithium triethylborohydride, after the apparent formation of complex **10**.

These results can be explained by assuming that the reaction of lithium trialkylborohydrides with 1,2-diols gives rise to the "ate" complexes **8** and **10**, which are stable in the absence of a proton source, while they expel, preferentially and rapidly, an alkyl group by internal (**8** ⟶ **10**) or external (**10** ⟶ **11**) protonation with a weak acid. Similarly, scrambling of the alkyl group of boronates with BuLi (experiment a) is likely to occur through the formation of the salt **10**.

In conclusion, the ready availability of reagents, simple reaction conditions and easy work-up procedure make this preparation of 2-alkyl-1,3,2-dioxaborolanes very attractive.

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