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Dichloroborane–dioxane: an exceptional reagent for the preparation of alkenyl- and alkylboronic acids

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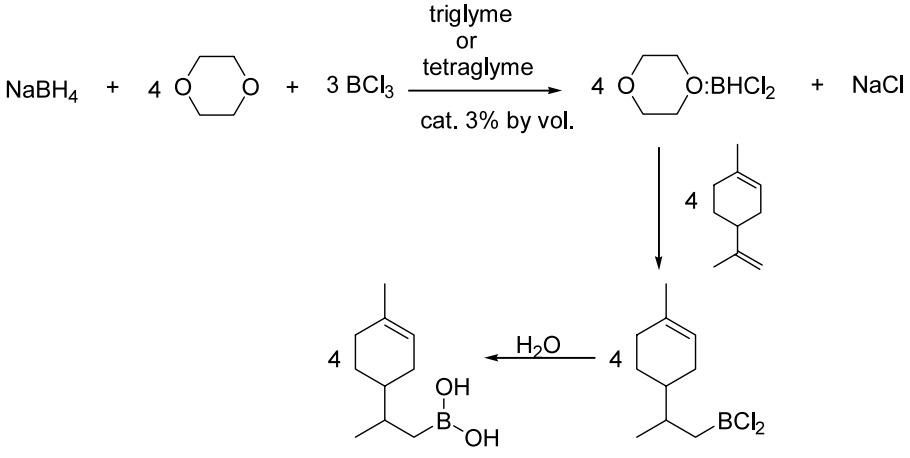
Abstract—Terminal alkynes and alkenes were conveniently hydroborated to the corresponding alkenyl- and alkyldichloroboranes using dichloroborane–dioxane in dichloromethane. These dichloroboranes were hydrolyzed by water to the corresponding alkenyl- and alkylboronic acids in moderate to good yields. With terminal alkenes and alkynes boron was predominantly attached to terminal carbon. Alkynes gave exclusively *trans*-vinylboronic acids.

Metal-mediated catalytic cross-coupling reactions continue to be widely practised in the synthesis of a broad range of compounds having applications in pharmaceutical, agrochemical, supramolecular and material science.[1] Among several available technologies, Suzuki–Miyaura coupling involving aryl-, alkenyl- and alkyl-boronic acids or esters with aryl-, heteroaryl halides or triflates has proven to be more effective and hence widely practised.[2] In recent years, a plethora of methodologies have been reported for the preparation of aryl- and heteroaryl-boronic acids or esters.[3] On the contrary, not much attention has been focussed on the preparation of alkyl- and alkenyl-boronic acids, in part due to the lesser reactivity of the alkylboronic acids in Suzuki–Miyaura coupling conditions.[4] Recently, there has been increased interest in developing Suzuki–Miyaura coupling conditions that can accommodate less reactive alkylboronic acids.[5,6]

Though alkenyl- and alkyl-boronic acids or esters can be prepared by several methods,[7] hydroboration of corresponding alkyne or alkene with catecholborane is the widely used method.[8] Unfortunately, the reaction of catecholborane with alkynes and alkenes is sluggish at room temperature, requiring high temperature (70°C for alkynes and 100°C for alkenes) and in some cases,



Scheme 1.

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isolation of product is complicated by the presence of catechol by-product. Though pinacolborane hydroborates alkynes to the corresponding alkenylpinacolborane esters at room temperature in 24 h, it requires two equivalents of pinacolborane and the method is not practical for the preparation of corresponding boronic acids, as these pinacol esters are highly stable towards hydrolysis and *trans*-esterifications.[9] Dibromoborane–methyl sulfide complex is a more practical reagent for the preparation of corresponding boronic acids from alkynes and alkenes. However, being a strong Lewis acid, dibromoborane may not be compatible with acid sensitive groups. Also, dimethyl sulfide is unpleasant to handle in large-scale applications.[10]

Recently, exceptional chloroborane complexes of dioxane were reported with interesting regio- and stereoselectivities, which are devoid of problems associated with earlier chloroborane reagents.[11] These complexes were prepared easily from simple inexpensive starting materials and are stable over an extended period of time at 0°C or room temperature. In particular, dichloroborane–dioxane exhibited interesting selectivities. In reaction with alkenes and alkynes, it gives the corresponding terminal dichloroboranes, which can be hydrolyzed to the corresponding boronic acids (Scheme 1).

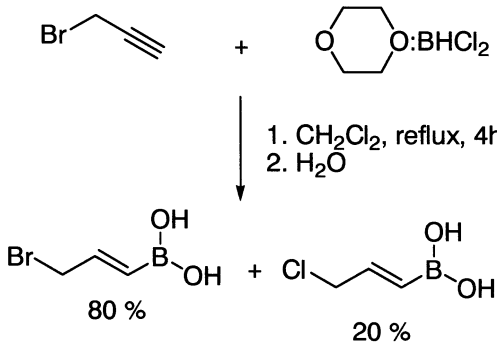
To further establish the synthetic potential of this promising reagent, we studied its reactivity towards representative alkynes and alkenes.[12] The addition of 1-octyne (0.11 mol) to a dichloromethane solution of dichloroborane–dioxane (3 M, 0.1 mol), resulted in an exothermic reaction and after 1 h, all 1-octyne is consumed as monitored by GC analysis. The reaction mixture was refluxed for another 4 h to ensure complete transformation. Hydrolysis of the resulting dichloroborane intermediate provided *E*-1-octen-1-ylboronic acid in 68% yield (Eq. (1)). The regio- and stereoisomeric purities were confirmed by ^{1}H NMR, which is consistent with the literature data.[8]

A number of alkynes and alkenes were hydroborated and hydrolyzed to the corresponding vinyl and alkylboronic acids in good yields. The results are summarized in Table 1.

Dichloroborane–dioxane hydroborates terminal alkynes conveniently to the corresponding vinyldichloroboranes in sterio- and regioselective manner. Even in the case of 3-chloro-1-propyne (entry 5), only terminal boron-addition product was isolated after workup and no internal addition product was noted in ^{1}H NMR.

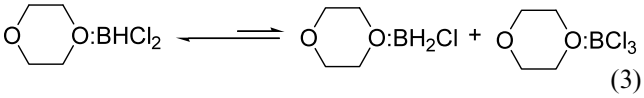
Hydroboration of internal alkynes under these conditions is sluggish. For example, the hydroboration of 3-hexyne (entry 6) with dichloroborane–dioxane gave only 15% of the expected product. Considerable amounts of unreacted 3-hexyne were noted in GC analysis. Similar reactivity patterns were also observed for olefins. More reactive cyclopentene and styrene gave the corresponding boronic acids in good yields (entries 7 and 8). However, moderately hindered cyclohexene (entry 9) gave lower yields (52%).

The hydroboration of 3-bromo-1-propyne gave an interesting side product. Under the reaction conditions shown (Eq. (2)), in addition to the expected *E*-bromomethyl vinylboronic acid considerable amounts of *E*-chloromethyl vinylboronic acid were also obtained.



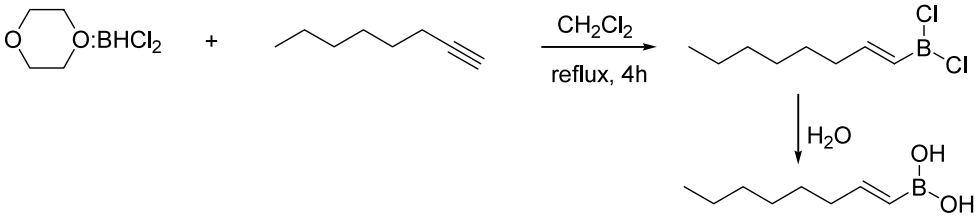
(2)

This is probably due to the halogen exchange resulting from dioxane–BCl_3 derived by the equilibration of dioxane–$BHCl_2$ under dichloromethane reflux conditions (Eq. (3)).[11a,13]



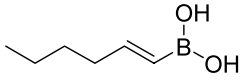
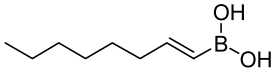
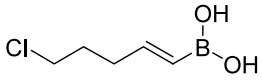
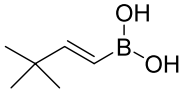
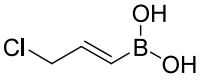
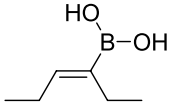
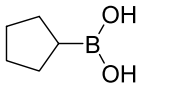
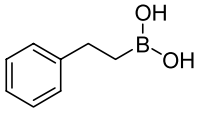
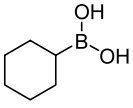
(3)

In conclusion, dichloroborane–dioxane shows exceptional reactivity in the hydroboration of terminal alkynes and alkenes. The corresponding dichloroboranes are conveniently converted to akenyl- and alkylboronic acids, which have high synthetic utility in metal mediated coupling reactions. The current reagent showed sluggish reactivity with internal alkynes. Further studies on improving its reactivity towards the broad spectrum of alkynes, alkenes and also utilizing its unique reactivity patterns in selective hydroboration are underway.



(1)

Table 1. Hydroboration-hydrolysis of alkynes and alkenes using dichloroborane–dioxane complex

Entry	Alkyne/alkene	Product[14]	Isolated Yield (%)
1	1-Hexyne		61
2	1-Octyne		71
3	5-Chloro-1-pentyne		67
4	3,3-Dimethyl-1-butyne		63
5	3-Chloro-1-propyne		68
6	3-Hexyne		15
7	Cyclopentene		62
8	Styrene		75
9	Cyclohexene		52

Acknowledgements

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12. Dichloroborane–dioxane complex, 3 M solution in dichloromethane is exclusively available from Aldrich Chemical Company (Cat # 55,595-9). General procedure: A nitrogen-flushed flask was charged with dichloroborane–dioxane in dichloromethane (3 M, 0.1 mol) under nitrogen pressure. Alkyne or alkene (0.11 mol) was added into the reaction flask dropwise using addition funnel under nitrogen. A vigorous reaction occurred and solvent started refluxing. After the addition was complete, the contents were refluxed for additional 4 h. The reaction mixture was cooled to 0°C with ice and water was added slowly drop wise. A vigorous reaction occurred with hydrogen chloride gas evolution. Dichloromethane was evaporated under reduced pressure and more water was added. The white solid precipitated was filtered and washed with water and cold pentane. The solid was dried under vacuum to obtain chemically pure boronic acid. Purity was checked using NMR and boron estimation.
13. To the best of our knowledge, such halogen exchange is not reported, though it is not unexpected for allylicbromides. Also, we observed similar halogen exchange for 2-bromomethylvinylboronic acid with boron trichloride in refluxing dichloromethane conditions.
14. All starting materials and products listed in the Table 1 are available from Aldrich Chemicals. 1-Hexyne (Cat # 24,442-2), 1-octyne (24,446-5), 5-chloro-1-pentyne (24,437-6), 3,3-dimethyl-1-butyne (24,439-2), 3-chloro-1-propyne (38,432-1), 3-hexyne (30,689-4), cyclopentene (34,450-8), α-styrene (24,086-9), cyclohexene (24,099-0), *E*-1-hexen-1-ylboronic acid (52,101-9), *E*-1-octen-1-ylboronic acid (52,102-7), *E*-5-chloro-1-pentenboronic acid (56,279-3), E-*tert*-butyl vinyl boronic acid (55,655-6), *E*-2-chloromethyl vinyl boronic acid (55,659-9), cyclopentylboronic acid (58,841-5), phenethylboronic acid (58,842-3), cyclohexylboronic acid (55,658-0), *E*-bromomethyl vinyl boronic acid (55,656-4).