New Methods of α-Bromination of Organoboranes in the Presence of Water. Convenient and General Synthesis of Highly Substituted Tertiary Alcohols

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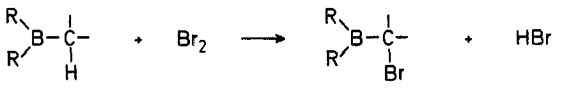
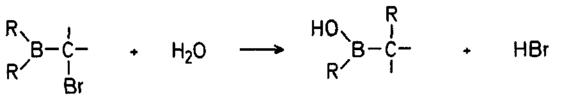
The reaction of organoboranes, such as trialkylboranes[1], dialkylborinic acids[2], and thexyldialkylboranes[3], with molecular bromine in the presence of water provides a new synthetic approach to the synthesis of carbon structures. These reactions involve, as the first stage, a free radical substitution in the α-position to produce an α-bromoorganoborane and hydrogen bromide[1,4].



$$\mathrm{RR'B{-}\underset{H}{\overset{|}{C}}{-}} + \mathrm{Br_2} \longrightarrow \mathrm{RR'B{-}\underset{Br}{\overset{|}{C}}{-}} + \mathrm{HBr}$$

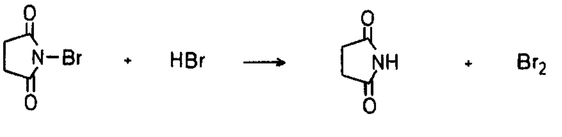
The α-bromoorganoborane undergoes a remarkably facile rearrangement under the influence of nucleophilic[4] and electrophilic catalysts[5]. Water is the most effective, causing a virtually instantaneous rearrangement[4].



$$\mathrm{RR'B{-}\underset{Br}{\overset{|}{C}}{-}} + \mathrm{H_2O} \longrightarrow \mathrm{HO(R')B{-}\underset{|}{\overset{R}{C}}{-}} + \mathrm{HBr}$$

To effect a successful α-bromination-migration, it is important to add molecular bromine slowly, in order to minimize polybromination of the original organoboranes. Furthermore, it is somewhat troublesome to measure and introduce molecular bromine quantitatively. Consequently, it appeared to us that the development of an alternative method which utilized a more readily handled bromine source or which permitted the automatic slow generation of bromine *in situ* would be helpful in overcoming these difficulties in handling molecular bromine itself.

Accordingly, we explored the reaction of typical organoboranes with N-bromosuccinimide (NBS) in the presence of water. It had been known that bromine is produced in the reaction medium in very small concentrations by the interaction of N-bromosuccinimide with hydrogen bromide[6].



In the bromination reaction, hydrogen bromide is produced as a by-product. Therefore, it appeared possible to utilize NBS to generate bromine *in situ*, slowly and automatically, for the α-bromination.

The results proved quite satisfactory (Table). For example, the reaction of triethylborane (10 mmol) with NBS (22 mmol) produced 3-methyl-3-pentanol, the double migrated alcohol, in 97% yield (9.7 mmol). This compares with an 85% yield for the reaction with molecular bromine[1]. The higher yield realized in the reaction with NBS is presumed to be due to the slow controlled generation of bromine.

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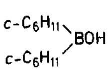
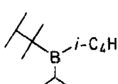
Table. Bromination of Organoboranes in the Presence of Water

Organoboranes (10 mmol)	Brominating reagents (mmol)	Products (%)[a]	
		Double migrated alcohol	Single migrated alcohol
		3-Methyl-3-pentanol	2-Butanol
$(C_2H_5)_3B$	NBS[b] (11)	43	12
	(22)	97 (98)[c]	
	$NaBrO_3$ (3.5)	41	12
	(7)	92	
		5-Propyl-5-nonanol	4-Octanol
$(n\text{-}C_4H_9)_3B$	NBS (11)	35	20
	(22)	78	
	$NaBrO_3$ (7)	76	
		4-Ethyl-3,4,5-trimethyl-3-heptanol	3,4-Dimethyl-3-hexanol
$(sec\text{-}C_4H_9)_3B$	NBS (11)		85
	(22)	62	37
	$NaBrO_3$ (3.5)		83
			1-Cyclohexylcyclohexanol
 $(c\text{-}C_6H_{11})_2BOH$	NBS (11)		98
	$NaBrO_3$ (3.5)		95
			1-(*i*-Butyl)-cyclopentanol
	NBS (11)		82
	$NaBrO_3$ (3.5)		80

[a] By G.L.C. analysis, based on organoboranes.

[b] N-bromosuccinimide.

[c] NBS was added slowly.

Sodium bromate was also utilized to introduce bromine *in situ*, slowly and automatically. This reagent reacts with hydrogen bromide to generate bromine[7].

$$NaBrO_3 + 6\,HBr \longrightarrow NaBr + 3\,Br_2 + 3\,H_2O$$

Indeed, this bromination system also achieved the α-bromination-migration reaction quite efficiently (Table).

The reaction of organoboranes with other brominating reagents, such as bromotrichloromethane[8] and 1,2-dibromo-1,1,2,2-tetrachloroethane, in the presence of water was also investigated briefly. However, these reagents did not appear to have any advantage over NBS or sodium bromate for this preparation of highly substituted tertiary alcohols.

Reaction of Triethylborane with N-Bromosuccinimide:

A 100-ml flask, equipped with a septum inlet, magnetic stirrer, and reflux condenser was charged with N-bromosuccinimide (4.0 g, 22 mmol), dichloromethane (20 ml), and water (10 ml). The flask was flushed with nitrogen and cooled with an ice bath. Then, triethylborane (1.42 ml, 10 mmol) was added and the resultant mixture was stirred. After the bromine color had disappeared (50–60 min), 3 *N* aqueous sodium hydroxide (10 ml) and ethanol (20 ml) were added at 0–5° followed by 30% aqueous hydrogen peroxide (3.3 ml). The resultant mixture was refluxed for 1 hr, and the organic layer was isolated and dried with potassium carbonate. G.L.C. analysis showed the presence of 9.7 mmol (97%) of 3-methyl-3-pentanol.

Reaction of Triethylborane with Sodium Bromate:

The same flask as above was charged with sodium bromate (1.06 g, 7 mmol), dichloromethane (20 ml), and water (10 ml). The flask was flushed with nitrogen and cooled with an ice bath. Then, triethylborane (1.42 ml, 10 mmol) was added and the mixture was stirred. *To start the reaction*, 48% *aqueous hydrogen bromide* (0.6 ml, 5 mmol) was added. After the same procedure as above had been employed, G.L.C. analysis indicated the presence of 9.2 mmol (92%) of 3-methyl-3-pentanol.

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