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Thexylhaloborane-Methyl Sulfide as Monohydroboration Reagent. Directive Effects in the Hydroboration of Alkynes

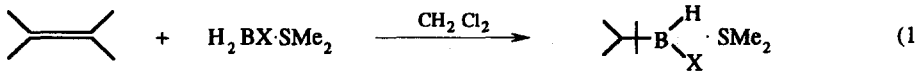
Jin Soon Cha*, Soo Jin Min, Jong Mi Kim, and Oh Own Kwon

Department of Chemistry, Yeungnam University, Kyongsan 712-749, Republic of Korea

Summary : Thexylhaloborane-Methyl sulfide, ThxBHX·SMe_2 (X= Cl, Br, I), undergoes direct hydroboration of both terminal and internal alkynes at 25 °C to provide the corresponding alkenyl-thexylhaloboranes in the exceptional isomeric purity.

Thexylchloroborane-methyl sulfide(ThxBHCl·SMe_2) is an exceptionally valuable reagent for the selective hydroboration of alkenes of different structural types.[1,2] This reagent hydroborates most olefins cleanly with high regio- and stereospecificity to produce isomerically pure thexylalkylchloroboranes.[3] This valuable monohydroborating ability of the reagent prompted an investigation of the reaction with alkynes. Thus, the directive effect in the monohydroboration of alkynes with ThxBHX·SMe_2 (X= Cl, Br, I) was examined as a potential route to synthesize isomerically pure aldehydes and ketones from alkynes.

ThxBHX·SMe_2 is readily prepared by hydroboration of 2,3-dimethyl-2-butene with the corresponding monohaloborane-methyl sulfide at 0 or 25 °C (*eq.*1).[1-4, 12]

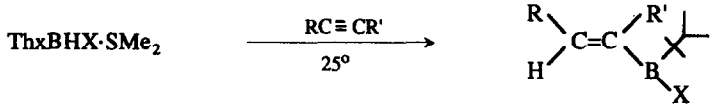


(1)

(X= Cl, Br, I)

Initially, the rate and stoichiometry of the reaction of ThxBHX·SMe_2 with representative terminal and internal alkynes were investigated. Stoichiometric amounts of the alkynes and ThxBHX·SMe_2 were employed in CH_2Cl_2 solution at 25 °C. The results reveal that, in general, the terminal alkynes undergo hydroboration at a rate slightly faster than the internal alkynes. The relative rate of hydroboration with ThxBHX·SMe_2 toward alkynes depends on the steric and electronic nature of the reagents, as anticipated. Thus, the rate is in order of ThxBHCl·SMe_2 > ThxBHBr·SMe_2 >> ThxBHI·SMe_2. All the terminal and internal alkynes examined undergo the hydroboration readily with ThxBHCl·SMe_2, ThxBHBr·SMe_2 and ThxBHI·SMe_2 at 25 °C in the stoichiometric ratio (1:1).

Especially noteworthy is the hydroboration of alkynes with excess ThxBHX·SMe_2. All the reagents even in an excess amount undergo a clean monohydroboration with either internal or terminal alkynes at 25 °C.



The directive effect of various unsymmetrically substituted acetylenes toward ThxBHX·SMe_2 was next investigated. The regiospecificity for the addition of ⟩BH was determined by oxidation of the intermediate alkenylthexylhaloboranes with hydrogen peroxide. The distribution of carbonyl isomers was then quantified by GC analysis. The results are summarized in Table 1.

Table 1. Directive Effects in the Monohydroboration of Alkynes with Thexyhaloborane-Methyl Sulfide in Methylene Chloride at 25 °C

Alkyne	Products	Product Distribution, % [a,b]		
		ThxBHCl·SMe_2	ThxBHBr·SMe_2	ThxBHI·SMe_2
1-hexyne	hexanal	97.0	99.0	99.0
	2-hexanone	3.0	2.0	1.0
1-heptyne	heptanal	98.0	99.0	>99.9
	2-heptanone	2.0	1.0	trace
2-hexyne	2-hexanone	98.0	98.5	99.0
	3-hexanone	2.0	1.5	1.0
3,3-dimethyl-1-butyne	trimethylacetaldehyde	99.0	>99.7	>99.9
	3,3-dimethyl-2-butanone	1.0	trace	trace
4,4-dimethyl-2-pentyne	4,4-dimethyl-2-pentanone	99.0	99.5	>99.9
	4,4-dimethyl-2-pentanone	1.0	0.5	trace
phenylethyne	phenylacetaldehyde	98.0	99.0	99.0
	acetophenone	2.0	1.0	1.0
1-phenyl-1-propyne	1-phenyl-2-propanone	3.0	1.0	1.0
	1-phenyl-1-propanone	97.0	98.0	99.0

a) The distribution is deduced by GC analysis from the oxygenated products of the intermediate alkenylboranes.
b) Total yields are 90 ± 5 %.

The results reveal that all the thexylhaloboranes achieve the clean monohydroboration of both internal and terminal alkynes with exceptional regioselectivity (> 97 % purity). Especially, in the case of hydroboration with ThxBHBr·SMe_2 and ThxBHI·SMe_2 almost perfect regioselectivity was realized at 25 °C. There is no significant difference in regioselectivity between internal and terminal alkynes. The reagents readily monohydroborate unsymmetrical alkynes to place the boron at the less hindered position.

	n - Bu - C ≡ C - H		*n* - Pr - C ≡ C - CH_3	
	↑	↑	↑	↑
ThxBHCl·SMe_2	3.0	97.0	2.0	98.0
ThxBHBr·SMe_2	2.0	98.0	1.5	98.5
ThxBHI·SMe_2	1.0	99.0	1.0	99.0

	Ph - C ≡ C - H		Ph - C ≡ C - CH_3	
	↑	↑	↑	↑
ThxBHCl·SMe_2	3.0	97.0	2.0	98.0
ThxBHBr·SMe_2	2.0	98.0	1.5	98.5
ThxBHI·SMe_2	1.0	99.0	1.0	99.0

Results for 2-hexyne and 1-phenyl-1-propyne, representative 1-substituted propyne derivatives, are presented in Tale 2 along with directive effects for several other hydroborating reagents for comparision.[4-9] The results indicate a prominent directive effect for ThxBHX·SMe_2, placing the boron at the least hindered

Table 2. Directive Effects (% Substitution) in 1-Subsituted Propynes

$$R\,C^{b} \equiv C^{a}CH_3$$

Hydroborating reagent	R			
	n-Pr		Ph	
	b	a	b	a
B_2H_6 [a,b]	40.0	60.0	74.0	26.0
$ThxBH_2$ [a,b]	39.0	61.0	43.0	57.0
$HBBr_2{\cdot}SMe_2$ [c]	25.0	75.0	64.0	36.0
catecholborane [d]	40.0	60.0	27.0	73.0
2,2'-biphenoxyborane [e]	39.0	61.0	16.0	84.0
9-BBN [f]	22.0	78.0	65.0	35.0
$CHex_2BH$ [a,b]	33.0	67.0	29.0	71.0
Sia_2BH [a,b]	39.0	61.0	19.0	81.0
$ThxBHCl{\cdot}SMe_2$	2.0	98.0	3.0	97.0
$ThxBHBr{\cdot}SMe_2$	1.5	98.5	1.0	99.0
$ThxBHI{\cdot}SMe_2$	1.0	99.0	1.0	99.0

a) Reference 4. b) Reference 5. c) Reference 6. d) Reference 7. e) Reference 8. f) Reference 9.

position. Comparison with other disubstituted boranes such as $HBBr_2{\cdot}SMe_2$,[6] 9-BBN,[9] 2,2'-biphenoxyborane,[8] and Sia_2BH,[4,5] reveals far superior regioselectivity for $ThxBHX{\cdot}SMe_2$, apparently due to the steric and electronic nature of the reagents. Consequently, regiospecific hydroboration of $ThxBHX{\cdot}SMe_2$ provides a valuable synthetic route to isomerically pure aldehydes and ketones from alkynes. In fact, the reaction of 1-heptyne with 10 % excess $ThxBHI{\cdot}SMe_2$ at 25 °C afforded pure heptanal in a yield of 82 % (> 99.9 % purity, 94 % GC yield).

$$CH_3(CH_2)_4C{\equiv}CH \xrightarrow[25°,\ 12\ h]{ThxBHI{\cdot}SMe_2} \xrightarrow[2.\ buffer\ (pH\ 7)]{1.\ NaOH} \xrightarrow{H_2O_2} CH_3(CH_2)_4CH_2CHO$$

82 % (isol.), 94 % (GC)

$$Ph\text{-}C{\equiv}C\text{-}CH_3 \xrightarrow[25°,\ 12\ h]{ThxBHI{\cdot}SMe_2} \xrightarrow[H_2O_2]{NaOH} Ph\text{-}CH_2\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_3$$

95 % (GC)

The regioselectivity of hydroboration of unsymmetrically substituted alkynes with $ThxBHX{\cdot}SMe_2$ was determined by oxidizing the intermediate alkenylboranes to the corresponding carbonyl compounds with hydrogen peroxide, followed by GC analysis. The following procedure for analysis of 1-heptyne is representative. A 50 mL round-bottom flask equipped with magnetic stirring bar, septum-covered sidearm, and connector tube leading to a mercury bubbler was charged with 0.66 mL (0.482 g, 5.0 mmol) of 1-heptyne, 0.85 g of dodecane (5.0 mmol) and 1.5 mL of CH_2Cl_2. To this solution at 25 °C was added 2.0 mL of 2.50 M $ThxBHI{\cdot}SMe_2$ solution in CH_2Cl_2. After 12 h at 25 °C, the reaction mixture was cooled to 0 °C, neautralized with 2 mL of 2.5 N NaOH, followed by addition of 5 mL of buffer solution (pH 7). Then

the mixture was oxidized by adding 1.5 mL of 30 % H_2O_2 dropwise at 0 °C. The mixture was stirred for 2 h at 0 °C. Then the aqueous layer was saturated with K_2CO_3 and the organic layer was separated. Analysis of the organic layer by GC on a Carbowax 20 M capillary column (15 m) revealed the presence of > 99.9 % heptanal and trace of 2-heptanone in a total yield of 93 %.

On a large scale reaction, 50 mmol of 1-heptyne was treated with 55 mmol of ThxBHI·SMe_2 (10 % excess) for 12 h at 25 °C. After the buffered oxidation, the aqueous layer was saturated with NaCl and the organic layer was separated. The aqueous layer was extracted with ether (3 x 20 mL). The combined organic layer was dried over anhydrous $MgSO_4$, followed by removal of the volatile components. Distillation afforded 4.7 g of heptanal; bp 152-153 °C, n_D^{22} 1.4120. GC analysis showed > 99.9 % purity and the ^1H NMR spectrum agreed with that of an authentic sample.

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