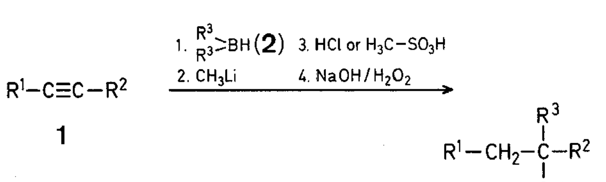
Novel Syntheses of Secondary and Tertiary Alcohols from Alkynes via the Hydroboration Reaction

George Zweifel and Richard P. Fisher

Department of Chemistry, University of California, Davis, California 95616, U.S.A.

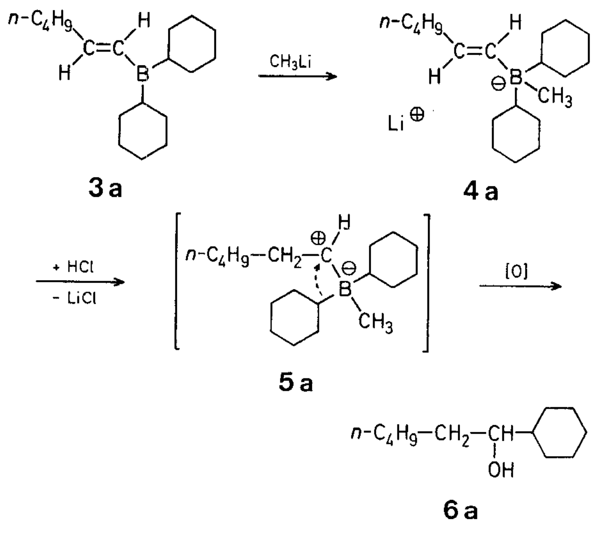
Protonation of lithium dialkylmethylvinylboronates with hydrogen chloride or methanesulfonic acid followed by oxidation of the resultant organoboranes affords secondary or tertiary alcohols in 70–80% yields. Combined with the syntheses of the lithium dialkylmethylvinylboronates, the overall reaction represents a conversion of mono- or disubstituted acetylenes (**1**) via stereoselective introduction of an alkyl group onto the triple bond, into the corresponding secondary or tertiary alcohols (**6**), respectively.



$$R^1{-}C{\equiv}C{-}R^2 \xrightarrow[2.\ CH_3Li \quad 4.\ NaOH/H_2O_2]{1.\ R^3_2BH\ (\mathbf{2}) \quad 3.\ HCl\ \text{or}\ H_3C{-}SO_3H} R^1{-}CH_2{-}C(R^3)(OH){-}R^2$$

1 **6**

Treatment of *trans*-1-hexenyldicyclohexylborane (**3a**) with hydrogen chloride resulted in extensive protonolysis of the vinyl C-B bond to produce 1-hexene. However, conversion of the vinylborane **3a** into the *ate* complex (**4a**) with methyllithium, followed by addition of an ethereal solution of hydrogen chloride (1 equiv), resulted in protonation of the double bond (**5a**) with concurrent migration of one cyclohexyl group from boron to the α-carbon[1]. This was evidenced by the disappearance of the vinyl protons in the ^{1}H-N.M.R. spectrum of the reaction mixture. Oxidation of the intermediate organoborane **5a** with alkaline hydrogen peroxide yielded 75% 1-cyclohexyl-1-hexanol (**6a**) along with 10% 1-hexene and 4% 2-heptanol[4].

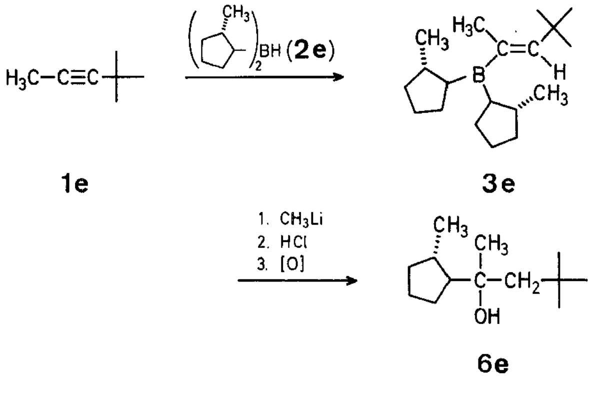


3a **4a** **5a** **6a**

It should be noted that migration of an alkyl group may also be accomplished using methanesulfonic acid instead of hydrogen chloride. However, slightly lower yields of alcohols were realized.

Of particular importance from a synthetic viewpoint is the fact that the migrating group retains its configuration. For example, 1-(*trans*-2-methylcyclohexyl)-1-hexanol (**6b**) was obtained through hydroboration of 1-hexyne with bis [*trans*-2-methylcyclohexyl]-borane (**2b**) followed by alkylation of boron, protonation, and oxidation.

Extension of the reaction to disubstituted alkynes provides a convenient synthesis of tertiary alcohols. It should be noted that dialkylboranes exhibit a marked regiospecificity in additions to the less hindered positions of unsymmetrically disubstituted acetylenes containing secondary and primary or tertiary and primary alkyl groups[5]. Thus, hydroboration of 4,4-dimethyl-2-pentyne (**1e**) with bis[*trans*-2-methylcyclopentyl]-borane (**2e**) places the boron nearly exclusively at the methyl-substituted carbon of the triple bond. Sequential treatment of the resultant dialkylvinylborane (**3e**) with methyllithium, hydrogen chloride, and alkaline hydrogen peroxide yields 2-(*trans*-2-methylcyclopentyl)-4,4-dimethyl-2-pentanol (**6e**).

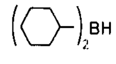
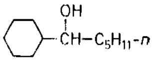
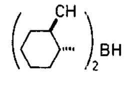
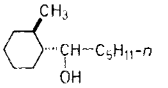
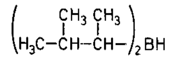
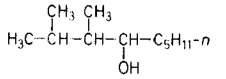
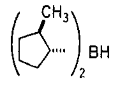
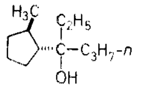
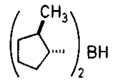
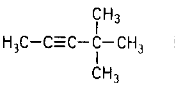
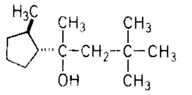


1e **3e** **6e**

A summary of the yields of alcohols (**6**) obtained in selected examples of these reactions is presented in the Table.

An interesting sidelight in these reactions is the low migratory aptitude of a methyl group as compared to a secondary alkyl group in the protonation of lithium dialkylmethylvinylboronates. Thus, in all examples reported in the Table, the amount of alcohol derived from migration of the methyl group was less than 5%. In this connection it is interesting to note that protonation of lithium cyclopentylmethylthexylvinylboronate, derived from hydroboration of 1-hexyne with thexylcyclopentylborane[9] followed by alkylation with methyllithium, resulted in migration of both the secondary and tertiary groups.

Table. Yields and Physical Properties of Alcohols (**6**) obtained from various Alkynes (**1**) and Dialkylboranes (**2**)

	2	**1**	Acid	**6**[a]	Yield (%) of Isolated **6**	b.p.	n_D
a		$HC\equiv C-C_4H_9$-*n*	HCl H_3C-SO_3H		69 65	83°/0.5 torr	$n_D^{24} = 1.4652$
b		$HC\equiv C-C_4H_9$-*n*	HCl H_3C-SO_3H		71[b,c] 64[b,c]	86°/1 torr	$n_D^{25} = 1.4656$
c	 $(H_3C-\underset{}{\overset{CH_3}{CH}}-\overset{CH_3}{CH}-)_2BH$	$HC\equiv C-C_4H_9$-*n*	HCl	 $H_3C-\overset{CH_3}{CH}-\overset{CH_3}{CH}-\underset{OH}{CH}-C_5H_{11}$-*n*	76[c]	76°/2 torr	$n_D^{24} = 1.4392$
d		$C_2H_5-C\equiv C-C_2H_5$	HCl		72[c,d]	68°/0.6 torr	$n_D^{24} = 1.4624$
e		 $H_3C-C\equiv C-\underset{CH_3}{\overset{CH_3}{C}}-CH_3$	HCl		79[c,d]	62°/1 torr	$n_D^{25} = 1.4607$

[a] The spectral and microanalytical data for all new compounds reported are consistent with the structures proposed.

[b] For structural assignment, see Ref.[6].

[c] Mixture of diastereomers.

[d] For structural assignment, see Ref.[8].

1-(*trans*-2-Methylcyclohexyl)-1-hexanol (6b):

To a solution of 1-methylcyclohexene (8.07 g, 84 mmol) in tetrahydrofuran (20 ml) was added dropwise a 2.07 *M* solution (20.3 ml, 42 mmol) of borane in tetrahydrofuran while maintaining the temperature at 0–10°. The reaction mixture containing insoluble dialkylborane **2b** was stirred at 0–5° for 4 h, then treated with a solution of 1-hexyne (3.28 g, 40 mmol) in tetrahydrofuran (20 ml), and stirred at 25° until the precipitate had dissolved (1 h). To the vinylborane (**3b**) thus formed was added at −70° a solution of methyllithium in ether (1.6 *M*, 44 mmol). After stirring for 15 min at −70°, the mixture was diluted with a freshly prepared solution of hydrogen chloride in ether (3.1 *M*, 48 mmol)[10]. After 15 min, the mixture was brought to room temperature (30 min) and stirred for an additional 30 min. The organoborane was oxidized at 35–50° by adding methanol (40 ml), 3*N* aqueous sodium hydroxide (25 ml), and 30% hydrogen peroxide (15 ml). After 15 min, the mixture was saturated with solid potassium carbonate (K_2CO_3 1.5 H_2O), and the organic phase formed was separated. The aqueous layer was extracted with ether, the combined extract washed once with saturated sodium chloride solution, dried with magnesium sulfate, and distilled; yield: 5.60 g (71%); b.p. 84–86°/1 torr; n_D^{25}: 1.4656[6].

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[1] The proton-induced migrations are reminiscent of the iodination[2] and cyanohalogenation[3] reactions of dialkylvinylboranes where the migration of an alkyl group from boron to the adjacent carbon is accompanied by a *trans* or *cis* deboronohalogenation to produce the corresponding *cis*- and *trans*-alkenes, respectively.

[2] G. Zweifel, H. Arzoumanian, C. C. Whitney, *J. Amer. Chem. Soc.* **89**, 3652 (1967).

[3] G. Zweifel, R. P. Fisher, J. T. Snow, C. C. Whitney, *J. Amer. Chem. Soc.* **94**, 6560 (1972).

[4] Treatment of alkynylboronates (Na[$R_3BC\equiv CR$]) with hydrogen chloride and hydrolysis of the resulting organoborane produced mixtures of the corresponding *cis*- and *trans*-alkenes: P. Binger, R. Köster, *Tetrahedron Lett.* **1965**, 1901.

[5] G. Zweifel, G. M. Clark, N. L. Polston, *J. Amer. Chem. Soc.* **93**, 3395 (1971).

[6] The product alcohol was oxidized to the ketone[7] which was then subjected to the Baeyer-Villiger degradation. Reduction of the ester obtained afforded exclusively *trans*-2-methylcyclohexanol and *n*-hexanol, thus establishing the *trans* configuration of the 2-methylcyclohexyl moiety.

[7] H. C. Brown, C. P. Garg, *J. Amer. Chem. Soc.* **83**, 2952 (1961).

[8] The structural assignment is based on the stereochemical result observed in the analogous reaction using bis[*trans*-2-methylcyclohexyl]-borane.

[9] E. Negishi, H. C. Brown, *Synthesis* **1972**, 196.

[10] Alternatively, the protonation may be carried out by using 48 mmol of methanesulfonic acid.