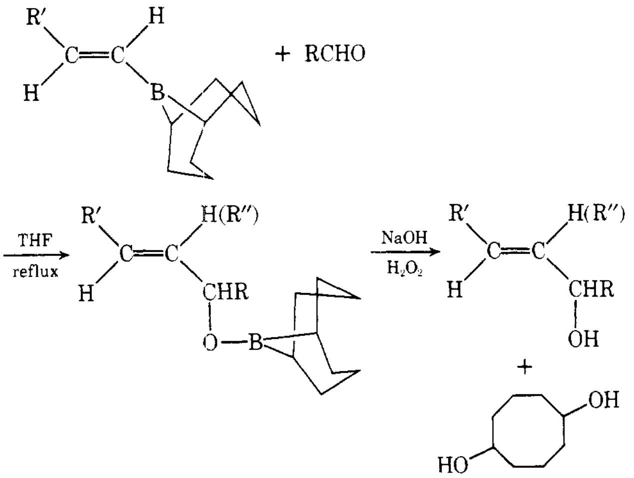
A Grignard-Like Addition of *B*-Alkenyl-9-borabicyclo[3.3.1]nonanes to Aldehydes, A Novel Synthesis of Allylic Alcohols with Defined Stereochemistry

Summary: *B*-Alkenyl-9-BBN derivatives add across the carbonyl group of representative aldehydes to give the corresponding allylic alcohols with the corresponding stereochemistry.

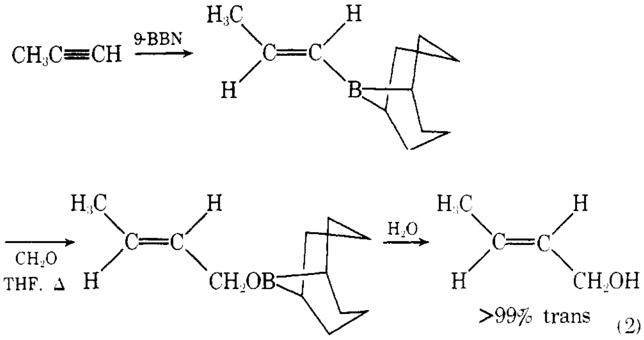
Sir: *B*-Alkenyl-9-borabicyclo[3.3.1]nonanes (*B*-alkenyl-9-BBN), in contrast to their saturated counterparts,[1] add across the carbonyl group of simple aldehydes. The products are the corresponding allylic alcohols (eq 1) with retained stereochemistry. Since the *B*-alkenyl-9-BBN derivatives are readily prepared by the hydroboration of acetylenes with 9-BBN,[2,3] this reaction sequence provides a remarkably simple synthesis of such allylic alcohols.



(1)

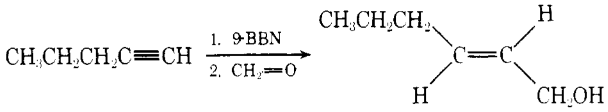
The reaction evidently proceeds with complete retention of the vinylborane stereochemistry. Thus, GC examination of the products reveals only a single peak. The ^{1}H NMR spectra are also consistent with the presence of only a single isomer. The IR spectra of the products derived from terminal acetylenes displayed a strong absorption at ~970 cm^{-1}, indicating the presence of a trans disubstituted olefinic linkage.[4] Consequently, it is highly probable that all of the reactions proceed with retention of configuration.

In one case, this conclusion was tested by comparing the product with authentic cis and trans isomers. Thus, propyne was treated with 9-BBN to form 1-propenyl-9-BBN,[5] which in turn was treated with formaldehyde. The product was crotyl alcohol, >99% trans by GC analysis (eq 2).



(2)

The addition of *B*-alkenyl-9-BBN to aldehydes appears to be a reaction of considerable generality (Table I). (The reaction of other alkenyldialkylboranes is less satisfactory.) A variety of simple aldehydes undergo the reaction. Furthermore, various substituents on the vinylborane moiety can be accommodated (eq 3–6).



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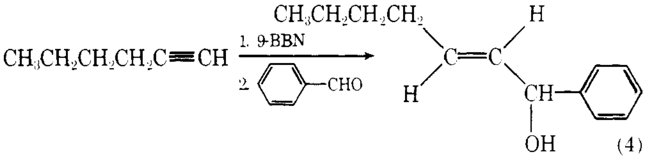

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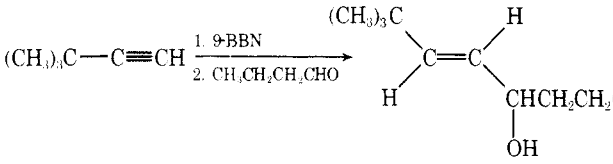
Table I. Coversion of Alkynes into Allylic Alcohols by the Reaction of the Corresponding *B*-Alkenyl-9-BBN Derivatives with Aldehydes[a]

Alkyne	Aldehyde	Product[b]	Yield,[c,d] %	$n^{20}\text{D}$
Propyne[e]	Formaldehyde[i]	*trans*-Crotyl alcohol	48	
1-Pentyne[f]	Formaldehyde[i]	*trans*-2-Hexen-1-ol	(36)	
1-Hexyne[g]	Benzaldehyde	1-Phenyl-*trans*-2-hepten-1-ol	86	1.5184
3,3-Dimethyl-1-butyne[h]	Butyraldehyde	7,7-Dimethyl-*trans*-5-octen-4-ol	(55)	1.4438
4,4-Dimethyl-2-pentyne[h]	Acetaldehyde	3,5,5-Trimethyl-*trans*-3-hexen-2-ol	69 (56)	1.4472
5-Chloro-1-pentyne[f]	Propionaldehyde	8-Chloro-*trans*-4-octen-3-ol	47	1.4718

[a] All reactions were carried out for 16 h in refluxing THF unless otherwise noted. [b] Satisfactory IR, ^{1}H NMR, and high resolution mass spectral data was obtained for all new compounds. [c] By GLC analysis. [d] Numbers in parentheses are isolated yields. [e] A 4-fold excess of propyne was used. [f] 100% excess alkyne was used. With straight-chain terminal alkynes, an excess is required to minimize dihydroboration. [g] Reaction was carried out for 2 h in refluxing toluene with distilled organoborane. [h] A 10% excess of the alkyne was used. [i] Monomeric formaldehyde was generated externally by the pyrolysis of paraformaldehyde.



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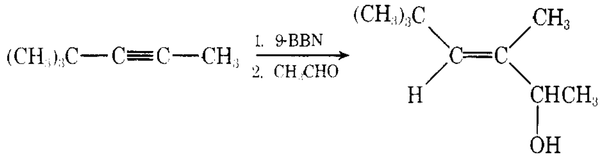
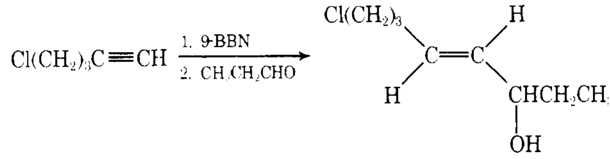


(6)

The following procedure is representative. An oven-dried 100-ml flask fitted with a reflux condenser and magnetic stirring bar was flushed with nitrogen and charged with 50 ml of 0.50 M 9-BBN[3] (25 mmol) in THF. To the solution was added 2.7 g (28 mmol) of 4,4-dimethyl-2-pentyne, and the solution was stirred overnight to ensure complete hydroboration. Acetaldehyde (2.2 g, 50 mmol[6]) was added, and the solution was heated under reflux for 16 h. After cooling to room temperature, the reaction mixture was oxidized by adding 15 ml of 3 N sodium hydroxide followed by the slow addition of 15 ml of 30% hydrogen peroxide (*Caution:* exothermic!). The solution was maintained at 50 °C to ensure complete oxidation. The aqueous layer was saturated with anhydrous potassium carbonate, separated, and extracted with hexane. The combined organic layer was dried over anhydrous magnesium sulfate and analyzed by GC, which indicated a 69% yield of 3,5,5-trimethyl-3-hexen-2-ol. Distillation provided 1.97 g (56%) of colorless liquid: bp 80–81 °C (12 mm); $n^{20}{}_{\mathrm{D}}$ 1.4472; IR (neat) 3350 cm^{-1}; ^{1}H NMR (CCl$_4$, TMS) δ 1.1–1.2 (s + d, 12 H), 1.7 (d, J = 1.5 Hz, 3 H), 4.1 (q, J = 6 Hz, 1 H), 5.4 (q, J = 1.5 Hz, 1 H).

Since the hydroboration reaction is known to be tolerant of a variety of functional groups,[5] we were intrigued with the possibility of achieving a "Grignard-like" synthesis with a reactive substituent present on the organometallic reagent. Thus, 5-chloro-1-pentyne was hydroborated with 9-BBN and then reacted with propionaldehyde to give *trans*-8-chloro-4-octen-3-ol (eq 7). Past experience with the application of such organoborane intermediates indicate that this reaction should accommodate many functional groups, such as ester and nitrile, providing chemists with a versatile new approach to the synthesis of functionalized allylic alcohols.



(7)

It should be emphasized that this communication describes an unexpected development. All previous attempts to achieve a Grignard-like reaction of organoboranes had failed.[1] Evidently, the present development provides a remarkably simple, stereospecific, synthetic route to allylic alcohols. Furthermore, there is the definite implication that such alkenylboranes will undergo other reaction types previously believed to be possible only with far more reactive organometallic compounds. This represents a promising new area.

References and Notes

(1) Heating *B*-*n*-butyl-9-BBN with benzaldehyde resulted in reduction of the carbonyl group: J. D. Buhler, Ph.D. Thesis, Purdue University, West Lafayette, Ind., 1973. In contrast, *B*-allyl-9-BBN (G. W. Kramer and H. C. Brown, manuscript in preparation) and other allylboranes readily add to the carbonyl groups: B. M. Mikhailov, *Organomet. Chem. Rev. A*, 1 (1972).

(2) H. C. Brown, E. F. Knights, and C. G. Scouten, *J. Am. Chem. Soc.*, **96,** 7765 (1974); C. G. Scouten, Ph.D. Thesis, Purdue University, West Lafayette, Ind., 1974.

(3) Available from Aldrich-Boranes, a subsidiary of the Aldrich Chemical Co.

(4) R. M. Silverstein and G. C. Bassler, "Spectrometric Identification of Organic Compounds", Wiley, New York, N.Y., 1975.

(5) The hydroboration of acetylenes involves a clean cis addition of the B–H bond: H. C. Brown, "Boranes in Organic Chemistry", Cornell University Press, Ithaca, N.Y., 1972; H. C. Brown, G. W. Kramer, A. B. Levy, and M. M. Midland, "Organic Syntheses via Boranes", Wiley-Interscience, New York, N.Y., 1975.

(6) Because of the high volatility of acetaldehyde (bp 21 °C), we employed a large excess. In most cases, the use of excess aldehyde is unnecessary.

(7) Graduate research assistant on grants provided by the National Science Foundation (GP-41169X) and by the G. D. Searle and Co. Chicago, Ill.

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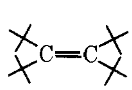
Tetraneopentylethylene

Summary: The highly hindered tetraneopentylethylene has been synthesized and was shown to exhibit a temperature dependent ^{1}H NMR spectrum demonstrating the nonequivalence of methylene protons, with the barrier of rotation across the sp^2–sp^3 bond being $\Delta G^{\ddagger} = 21.7 \pm 5$ kcal/mol at 145 °C.

Sir: In continuation of our studies on highly hindered olefins and their electrophilic reactions,[1,2] such as adamantylideneadamantane and homoadamantylidenehomoadamantane, the extremely hindered tetra-*tert*-butylethylene **1** would be of great interest, but it remains elusive despite efforts in different laboratories.[3] Recent methods developed by McMurry and Flemming[4] and their modifications[4d] for the reductive coupling of carbonyl compounds with low-valent titanium reagent has greatly facilitated attempts to prepare hindered olefins.[5-7] We wish now to report the synthesis of tetraneopentylethylene (**2**), one of the most crowded symmetrical tetraalkyl-substituted ethylenes.



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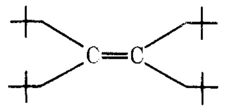

2

Tetraneopentylethylene, mp 59 °C, a white crystalline solid was obtained in 38% yield by the reductive coupling of dineopentyl ketone[7b] using titanium(II) reagent[2,4] in tetrahydrofuran solution. In a 500-ml three-necked flask fitted with a reflux condenser under nitrogen is weighed TiCl$_3$ (31.3 g, 0.2 mol); 200 ml of anhydrous THF is added to it under stirring, and the flask is cooled to −40 °C (dry ice/acetone bath). Under stirring LiAlH$_4$ (3.8 g, 0.1 mol) is added in portions; rapid gas evolution is seen. After the addition, the mixture is warmed to room temperature and refluxed for 1 h, dineopentyl ketone (16.8 g, 0.1 mol) in 50 ml of THF is added dropwise, and the mixture is refluxed for 8 h more. Then the mixture is cooled, poured over 10% ice-cold NH$_4$Cl solution, and worked up with ether in the usual manner. The product is purified by chromatography on alumina (petroleum ether eluent): ^{13}C NMR (25.1 MHz, CDCl$_3$, from capillary TMS, 37 °C) δ 136.56 (vinylic carbon), 47.36 (CH$_2$, J_{CH} = 121.0 Hz), 35.23)quaternary carbon), 32.47 (CH$_3$, J_{CH} = 128.1 Hz); mass spectrum (70 eV) (relative abundance) m/e 308 (78.1, M$^+$), 252 (40.6), 251 (50.2), 196 (30.2), 195 (63.8), 167 (11.2), 154 (7.7), 140 (18.7), 139 (58.3), 125 (20.6), 111 (15.8), 99 (10.5), 85 (11.4), 83 (19.6), 71 (13.0), 57 (100), 41 (24.3), 29 (15.7). Elemental Anal.[8a] Calcd for C$_{22}$H$_{44}$: C, 85.71; H, 14.29. Found: C, 85.76; H, 14.39.

Of particular interest is the marked temperature dependence of the ^{1}H NMR spectrum[8b] of **2.** The methylene protons show an AB pattern, centered at δ 2.18 (J_{AB} = 13.0 Hz) up to 104 °C; coalescence occurs at 145 °C. The methyl groups resonate at δ 0.97 as a singlet without any change with temperature. The appearance of two different methylene protons is