trans-myrtanol by VPC. After 4 h only a trace of the cis isomer remained.

Preparation of (+)-β-Pinene. A 100-mL reaction flask was charged with 27.5 mmol of 9-BBN (0.5 M) and 25 mmol of (+)-α-pinene, $[\alpha]^{25}_{D}$ +47.23° (92% ee). The solution was refluxed for 3 h and then the THF removed with a water aspirator. Diglyme (40 mL) was added and the solution refluxed for 30 h. After cooling, 25 mmol of freshly distilled benzaldehyde was added and the solution again heated to reflux for a brief time. The solution was cooled and oxidized with the addition of 9.5 mL of 3 N sodium hydroxide and 7 mL of 30% hydrogen peroxide. The mixture was stirred for 2 h at 40–50 °C, cooled to room temperature, and extracted with hexane. The hexane layer was washed several times with water and then with saturated sodium chloride. After drying over potassium hydroxide and concentrating, the crude product (56% VPC yield of β-pinene and 22% of α-pinene) was chromatographed on silica gel–silver nitrate (prepared from 180 g of silica gel and 20 g of silver nitrate in acetonitrile). Elution with 1% ethyl acetate in hexane gave 1.745 g (51.2%) of (+)-β-pinene, bp 45 °C (31 mmHg, Kugelrohr), $[\alpha]^{25}_{D}$ +19.59° (l = 1, neat) (lit.[13] $[\alpha]_{D}$ +22.8°).

Acknowledgment. We wish to thank the National Institutes of Health for financial support and the University of California, Riverside, for a President's Undergraduate Fellowship to S.A.Z.

Registry No. *B-trans*-2-Methylcyclopentyl-9-BBN, 63942-79-0; *B*-3-methyl-2-butyl-9-BBN, 63942-78-9; *B*-3-pinanyl-9-BBN, 64106-79-2; 1-octene, 111-66-0; 2-methyl-1-pentene, 763-29-1; styrene, 100-42-5; *p*-methoxystyrene, 637-69-4; cyclohexene, 110-83-8; 1-methylcyclohexene, 591-49-1; 2-methyl-1-pentanol, 105-30-6; *B-cis*-myrtanyl-9-BBN, 79919-20-3; *B-trans*-myrtanyl-9-BBN, 79919-21-4; (−)-β-pinene, 18172-67-3; 9-BBN, 280-64-8; (+)-α-pinene, 7785-70-8; (+)-β-pinene, 19902-08-0; *cis*-myrtanol, 51152-12-6; *trans*-myrtanol, 53369-17-8.

Hydroboration Kinetics. 3.[1] Kinetics and Mechanism of the Hydroboration of Alkynes with 9-Borabicyclo[3.3.1]nonane Dimer. Effect of Structure on the Reactivity of Representative Alkynes

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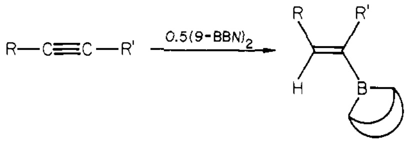
Contribution from the Richard B. Wetherill Laboratory, Purdue University, West Lafayette, Indiana 47907. *Received June 19, 1981*

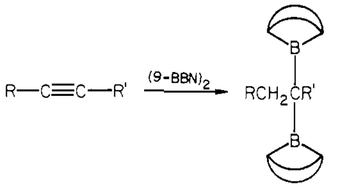
Abstract: The hydroboration of alkynes with 9-borabicyclo[3.3.1]nonane dimer, $(9\text{-BBN})_2$, exhibits kinetics similar to those for the hydroboration of alkenes. For the more reactive alkynes such as 1-hexyne, 3-methyl-1-butyne, 3,3-dimethyl-1-butyne, and cyclohexylethyne, the reaction exhibits first-order kinetics, first order in $(9\text{-BBN})_2$ only. For the less reactive alkynes, such as diphenylethyne, the reaction exhibits three-halves-order kinetics, first order in alkyne and one-half order in $(9\text{-BBN})_2$. Intermediate kinetics between first and three-halves order were observed with phenylethyne. Apparently the reaction proceeds through the same mechanism as the hydroboration of alkenes. There is a prior dissociation of the 9-BBN dimer into the monomer, followed by the reaction of the monomer with the alkyne. The relative reactivities of the alkynes toward 9-BBN, as well as the relative reactivities between the alkynes and their monohydroboration products, were obtained by competitive studies. The experimental results for the relative rates of mono- and dihydroboration of the alkynes are in very good agreement with the calculated numbers obtained by the use of the Runge–Kutta numerical method. This method is also used to predict the percentage of monohydroboration when an excess amount of alkyne is used.

The hydroboration of alkynes with 9-borabicyclo[3.3.1]nonane dimer, $(9\text{-BBN})_2$, has been shown to offer a convenient route to *B*-vinyl-9-BBN derivatives (eq 1), as well as to *gem*-dibora derivatives (eq 2.)[3] Both of these two derivatives are useful intermediates in organic synthesis.[4]

However, the hydroboration of alkynes with $(9\text{-BBN})_2$ has some unusual characteristics. In contrast to the disiamylborane dimer which reacts very rapidly with both terminal and internal alkynes,[5] the hydroboration of alkynes with $(9\text{-BBN})_2$ is rather sluggish. One can selectively hydroborate a terminal double bond in the presence of an internal triple bond (eq 3).[6]

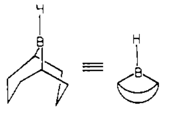


(1)



(2)

R′ = H or R, 9-BBN =



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(1) For previous studies in this series, see: (a) Brown, H. C.; Scouten, C. G.; Wang, K. K. *J. Org. Chem.* **1979**, *44*, 2589–2591. (b) Brown, H. C.; Wang, K. K.; Scouten, C. G. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *77*, 698–702. (c) Wang, K. K.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 5303–5306.

(2) (a) Graduate research assistant on Grant CHE 76-20846 of the National Science Foundation. (b) Graduate research Assistant on Grant GP-6942X of the National Science Foundation.

(3) Brown, H. C.; Scouten, C. G.; Liotta, R. *J. Am. Chem. Soc.* **1979**, *101*, 96–99.

(4) See ref 3 and references cited therein.

(5) Brown, H. C.; Moerikofer, A. W. *J. Am. Chem. Soc.* **1963**, *85*, 2063–2065.

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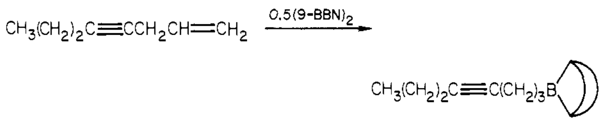
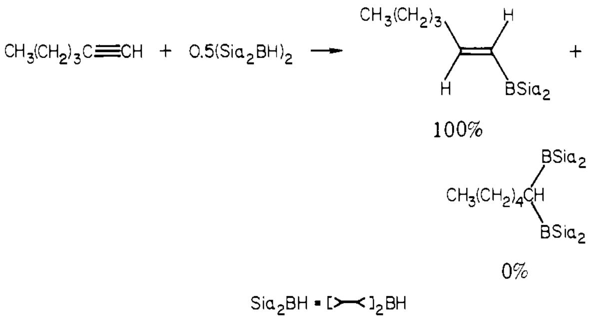


(3)

The hydroboration of a terminal alkyne with 0.5 equiv of disiamylborane dimer,[7] $(Sia_2BH)_2$, or dicyclohexylborane dimer[8] gives very cleanly the corresponding vinylborane derivatives (eq 4). However, a considerable amount of *gem*-dibora derivatives from dihydroboration of a terminal alkyne was observed with $(9\text{-BBN})_2$ (eq 5).[3]



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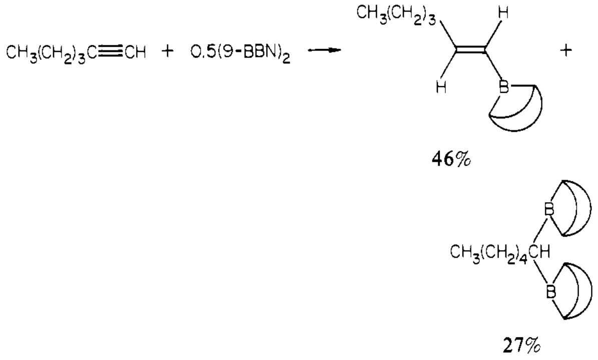


(5)

In view of these unusual characteristics, we therefore undertook a systematic kinetic study of the hydroboration of alkynes with $(9\text{-BBN})_2$ in order to unravel the reaction mechanism. This also provided a comparison with the mechanism for hydroboration of alkenes with $(9\text{-BBN})_2$, clearly established to proceed through prior dissociation of 9-BBN dimer into the monomer (eq 6), followed by the reaction of the monomer with the alkenes (eq 7).[1]

$$(9\text{-BBN})_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} 2(9\text{-BBN}) \qquad (6)$$

$$9\text{-BBN} + \text{alkene} \xrightarrow{k_2} B\text{-alkyl-9-BBN} \qquad (7)$$

In addition, the effect of structure of the reactivity of alkynes toward hydroboration with 9-BBN was studied. The phenomenon of the large percentage of dihydroboration was also investigated.

Results and Discussion

Kinetics and Mechanism. The kinetics of the hydroboration of alkynes with $(9\text{-BBN})_2$ were studied by adding various alkynes to the solutions of $(9\text{-BBN})_2$ in the solvent maintained at 25 °C. All operations were carried out under nitrogen until the analysis had been completed. Two different methods were used to follow the reaction.

In the first method,[1c] each reaction mixture was pumped through a sodium chloride infrared cell. The rate of the disappearance of the infrared absorption of the boron-hydrogen bridges of $(9\text{-BBN})_2$ at 1570 cm^{-1} was monitored by a quantitative infrared spectrometer. The absorbance was recorded on the chart paper of a recorder. In the second method,[1a,b] an aliquot of the reaction mixture was removed periodically, quenched with excess methanol, and analyzed by GLC for residual alkyne.

Table I. First-Order Rate Constants for the Hydroboration of Alkynes with $(9\text{-BBN})_2$ in Various Solvents at 25 °C

	10^4k_1, s^{-1}			
alkyne	THF	CCl_4	cyclohexane	benzene
1-hexyne	14.1	1.52	1.48	1.98
3-methyl-1-butyne	14.0			
cyclohexylethyne	14.3			
3,3-dimethyl-1-butyne	13.9			

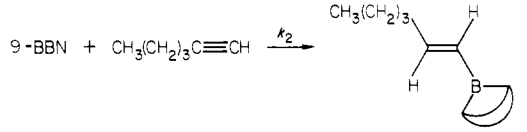
First-Order Kinetics. The hydroboration of 1-hexyne with $(9\text{-BBN})_2$ in CCl_4 at 25 °C exhibits first-order kinetics, first order in $(9\text{-BBN})_2$ only (eq 8). The first-order rate constant is 1.52

$$-\frac{d[(9\text{-BBN})_2]}{dt} = k_1[(9\text{-BBN})_2] \qquad (8)$$

$\times\ 10^{-4}\ s^{-1}$ (Table I). This number is in very good agreement with the first-order rate constant, $k_1 = 1.54 \times 10^{-4}\ s^{-1}$, observed for the hydroboration of 1-hexene with $(9\text{-BBN})_2$.[1] Apparently, the mechanism of the hydroboration of 1-hexyne with $(9\text{-BBN})_2$ is very similar to that of 1-hexene. The reaction proceeds through prior dissociation of the 9-BBN dimer into the monomer (eq 9),

$$(9\text{-BBN})_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} 2(9\text{-BBN}) \qquad (9)$$

followed by the subsequent reactions of the 9-BBN monomer with the substrates. The dissociated 9-BBN monomer may react either with 1-hexyne (eq 10) or with the monohydroborated product, *B*-(*trans*-1-hexen-1-yl)-9-BBN (eq 11).



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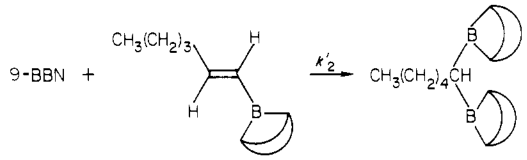

(11)

As in the case of 1-hexene, the dissociation of the 9-BBN dimer (eq 9) is the rate-determining step. One additional subsequent reaction pathway (eq 11) will only help to deplete the dissociated 9-BBN monomer and make the dissociation of the dimer more of a rate-determining step. Therefore, the rate of the disappearance of $(9\text{-BBN})_2$ monitored by the quantitative IR spectrometer for the reaction with 1-hexyne is essentially identical with that of 1-hexene.

Solvent Effects. The effects of solvent on the first-order rate constant of the hydroboration of 1-hexyne are also very similar to those of 1-hexene.[1] A list of the first-order rate constants for 1-hexyne in CCl_4, cyclohexane, benzene, and tetrahydrofuran (THF) is given in Table I. Clearly, in these solvents the rate of the dissociation of the 9-BBN dimer is the rate-determining step.

A much larger first-order rate constant in THF solvent is again observed. This is certainly of great interest. A detailed discussion will be given later.

Structure Effects. Several additional terminal alkynes, such as 3-methyl-1-butyne, 3,3-dimethyl-1-butyne, and cyclohexylethyne, were studied in THF solvent. The rates of the disappearance of $(9\text{-BBN})_2$ were again monitored with an IR spectrometer. Like 1-hexyne, they all exhibited first-order kinetics (Table I). Very good agreement between these first-order rate constants was realized. Apparently, for these terminal alkynes, the dissociation of $(9\text{-BBN})_2$ (eq 9) is the rate-determining step. The insensitivity of the reaction rate to changing the structure of the alkyne constitutes another persuasive evidence for the

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(6) Brown, C. A.; Coleman, R. A. *J. Org. Chem.* **1979**, *44*, 2328–2329.
(7) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 3834–3840.
(8) Zweifel, G.; Clark, G. M.; Polston, N. L. *J. Am. Chem. Soc.* **1971**, *93*, 3395–3399.

proposed dissociation mechanism.

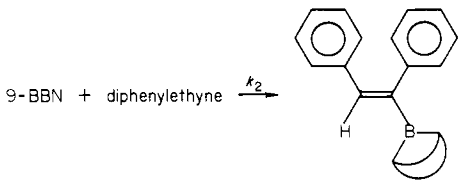
Three-Halves-Order Kinetics. The rate of the hydroboration of diphenylethyne with $(9\text{-BBN})_2$ is slower than that of 1-hexyne in CCl_4 at 25 °C. The reaction exhibits three-halves-order kinetics, first order in diphenylethyne and one-half order in $(9\text{-BBN})_2$ (eq 12).

$$-\frac{d[(9\text{-BBN})_2]}{dt} = k_{3/2}[(9\text{-BBN})_2]^{1/2}[\text{diphenylethyne}] \qquad (12)$$

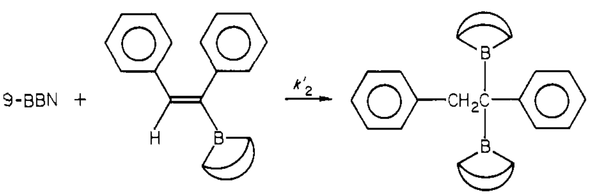
$$k_{3/2} = 1.3 \times 10^{-6}\ M^{-1/2}\ s^{-1}$$

Apparently, the subsequent reactions of the dissociated 9-BBN monomer (eq 13) with diphenylethyne (eq 14) and *B*-(*cis*-1,2-diphenylethenyl)-9-BBN (eq 15) become the slow steps.

$$(9\text{-BBN})_2 \overset{k_1}{\underset{k_{-1}}{\rightleftharpoons}} 2(9\text{-BBN}) \qquad (13)$$



(14)



(15)

If diphenylethyne and *B*-(*cis*-1,2-diphenylethenyl)-9-BBN have similar reactivities toward the 9-BBN monomer, the reaction kinetics will be complicated. The reaction then can be regarded as a competitive, consecutive second-order reaction.[9] Therefore, no simple integrated kinetic rate expression can be derived. Fortunately, the reaction rate of 9-BBN monomer with *B*-(*cis*-1,2-diphenylethenyl)-9-BBN is much slower than that of diphenylethyne. No dihydroboration adduct was observed. Therefore, ignoring eq 15 becomes a reasonable approximation. Consequently, as in the case of cyclohexene, three-halves-order kinetics were observed.[1]

Intermediate Kinetics. The reaction rate of the hydroboration of phenylethyne with $(9\text{-BBN})_2$ in CCl_4 at 25 °C is between that of 1-hexyne and diphenylethyne. The kinetic data fit neither first-order nor three-halves-order integrated rate expressions. Apparently, for phenylethyne, the rate of the dissociation of $(9\text{-BBN})_2$ is about the same as that of the subsequent reactions. Therefore, the reaction exhibits intermediate kinetic behavior between that of first- and three-halves-order kinetics.

Relative Reactivities. Although the hydroboration of 1-hexyne, 3-methyl-1-butyne, 3,3-dimethyl-1-butyne, and cyclohexylethyne all exhibit the same first-order rate of reaction, they have very different relative reactivities toward 9-BBN (Table II). Since for these alkynes the rate of the dissociation of $(9\text{-BBN})_2$ is the rate-determining step (eq 9), their relative reactivities must be measured by using the competitive method. In this method, a solution containing an equimolar amount of an alkene and an alkyne was reacted with 0.5 equiv of $(9\text{-BBN})_2$.[1b] After the reaction was completed, the unreacted starting materials were analyzed by GLC. Typically, a more reactive alkene, such as 1-heptene, was chosen to compare with a less reactive alkyne, such as 1-hexyne. Such an indirect comparison instead of a direct comparison of two terminal alkynes will greatly minimize the complication from dihydroboration.

The relative reactivities obtained by the competitive studies are the relative values of the k_2's of these alkynes (eq 10). The fact that these alkynes have very different values for k_2 (Table II) and yet have almost identical values for k_1 further supports the proposed dissociation mechanism.

Table II. Relative Reactivities of Representative Alkynes and Alkenes toward $(9\text{-BBN})_2$, $(Sia_2BH)_2$, and $HBBr_2{\cdot}SMe_2$

	relative reactivity[a]		
alkyne or alkene	$(9\text{-BBN})_2$[b]	$(Sia_2BH)_2$[c]	$HBBr_2{\cdot}SMe_2$[d]
1-hexene	100	100	100[e]
cis-3-hexene	0.68	1.85	20[f]
1-hexyne	15.3	373	290
1-decyne	18		
3-methyl-1-butyne	48.5		
3,3-dimethyl-1-butyne	86		
cyclohexylethyne	41		
phenylethyne	1.41		
3-hexyne	0.64	225	5900
4,4-dimethyl-2-pentyne	0.63		
diphenylethyne	1.77×10^{-3}		

[a] Normalized; 1-hexene = 100. [b] Reference 10; in THF at 25 °C. [c] Reference 5; in THF at 0 °C. [d] Reference 11; in CH_2Cl_2 at 25 °C. [e] 1-Octene. [f] *cis*-4-Octene.

It is clear from Table II that in a terminal alkyne, branching of the alkyl group at the 3-position, unlike the corresponding alkene, increases the relative reactivity in the following order: 1-hexyne < 3-methyl-1-butyne < 3,3-dimethyl-1-butyne. On the other hand, the relative reactivity of the corresponding alkene decreases with branching at the 3-position in the following order: 1-hexene > 3-methyl-1-butene > 3,3-dimethyl-1-butene.[10]

Since the hydroboration of diphenylethyne with $(9\text{-BBN})_2$ is slower than that of 1-hexyne and exhibits three-halves-order kinetics, the relative reactivity of diphenylethyne should be much smaller than that of 1-hexyne. Indeed, this is the case. Phenylethyne, which exhibits intermediate kinetic behavior, should have a relative reactivity between that of 1-hexyne and diphenylethyne. Indeed, this is also observed.

Unlike other hydroborating agents, such as disiamylborane dimer[5] and dibromoborane–dimethyl sulfide complex,[11] $(9\text{-BBN})_2$ does not exhibit large increases of relative reactivity toward alkynes. In fact, the relative reactivity of 1-hexyne is only about one-seventh that of 1-hexene, and 3-hexyne exhibits about the same relative reactivity as *cis*-3-hexene. This allows one to selectively hydroborate a terminal alkene in the presence of an internal alkyne as was observed previously[6] (eq 3).

Relative Rates between Mono- and Dihydroboration. In contrast to the disiamylborane dimer[7] and the dicyclohexylborane dimer,[8] the hydroboration of a terminal alkyne, such as 1-hexyne, with 1 equiv of 9-BBN in terms of the monomer produces a considerable amount of the *gem*-dibora derivative (eq 5).[3] Presumably, the ratio between k_2 (eq 10) and k_2' (eq 11) for terminal alkynes is relatively small. However, for an internal alkyne, no significant dihydroboration was observed.[3] Presumably, the ratio between k_2 and k_2' for an internal alkyne is much larger.

The relative rate (k_2/k_2') between mono- and dihydroboration of an alkyne with $(9\text{-BBN})_2$ was also studied by the competitive method. The *B*-vinyl-9-BBN, such as *B*-(*trans*-1-hexen-1-yl)-9-BBN from 1-hexyne, was prepared and isolated.[3] However, the relative reactivity between 1-hexyne and *B*-(*trans*-1-hexen-1-yl)-9-BBN was not compared directly. A direct comparison would make the analysis very complicated, because *B*-(*trans*-1-hexen-1-yl)-9-BBN would also be produced from 1-hexyne during the reaction. This difficulty was again circumvented by the use of an indirect route in which *B*-(*trans*-1-hexen-1-yl)-9-BBN was compared with an alkene. Since the relative reactivity of 1-hexyne and the alkene had been obtained previously, the ratio of k_2/k_2' could be calculated.

3,3-Dimethyl-1-butene was chosen to compare with *B*-(*trans*-1-hexen-1-yl)-9-BBN. It was observed that 3,3-dimethyl-1-butene

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(9) Frost, A. A.; Pearson, R. G. "Kinetics and Mechanism", 2nd ed; Wiley: New York, 1961.

(10) Brown, H. C.; Liotta, R.; Scouten, C. G. *J. Am. Chem. Soc.* **1976**, *98*, 5297–5301.

(11) Brown, H. C.; Campbell, J. B., Jr. *J. Org. Chem.* **1980**, *45*, 389–395.

Table III. Relative Rates between Mono- and Dihydroboration of Alkynes with $(9\text{-BBN})_2$ in THF at 25 °C

alkyne	relative rate, k_2/k_2'
1-hexyne	1.92
3-hexyne	193

was about 2.96 times more reactive than *B*-(*trans*-1-hexen-1-yl)-9-BBN.[12] The previous study indicated that 3,3-dimethyl-1-butene was 1.54 times more reactive than 1-hexyne (Table II).[1b] Therefore, the relative reactivity (k_2/k_2') between 1-hexyne and *B*-(*trans*-1-hexen-1-yl)-9-BBN could be calculated as 2.96/1.54 = 1.92. A similar comparison between 3-hexyne and *B*-(*cis*-3-hexen-3-yl)-9-BBN was also studied. The ratio was found to be 193. A list of these data is given in Table III.

Correlation between k_2/k_2' and the Percentage of Monohydroboration. It is clear from Table III that the small difference between k_2 and k_2' in 1-hexyne can account for its high percentage of dihydroboration. On the other hand, the large difference between k_2 and k_2' of 3-hexyne can explain its much lower percentage of dihydroboration. In fact, the percentages of mono- and dihydroboration are in direct correlation with k_2/k_2'. One should be able to predict the percentages of mono- and dihydroboration from the value of k_2/k_2'. A computer program using the Runge–Kutta numerical method[13] was written to establish this relationship.

As was described previously, the subsequent reactions of the 9-BBN monomer with an alkyne (eq 10) and its corresponding *B*-vinyl-9-BBN (eq 11) can be regarded as competitive, consecutive second-order reactions.[9] This is a complex kinetic situation and has been the subject of numerous investigations. The particular difficulty here is that the reaction steps are second order (eq 16 and 17). The integrated rate expressions of eq 16 and 17 cannot be obtained.

$$d[B\text{-vinyl-9-BBN}]/dt = k_2[\text{9-BBN}][\text{alkyne}] - k_2'[\text{9-BBN}][B\text{-vinyl-9-BBN}] \quad (16)$$

$$d[gem\text{-dibora-9-BBN}]/dt = k_2'[\text{9-BBN}][B\text{-vinyl-9-BBN}] \quad (17)$$

However, these differential equations can be very easily integrated by the use of the Runge–Kutta numerical method with the help of a digital computer to calculate the final concentrations of *B*-vinyl-9-BBN and *gem*-dibora-9-BBN derivatives. The relative values of k_2 and k_2', such as 1.92 and 1 for 1-hexyne, were substituted into eq 16 and 17. The concentration of the 9-BBN monomer was arbitrarily assigned as 1, because the 9-BBN monomer term would cancel out between eq 16 and 17. The d*t* was first assigned as 0.1. The concentrations of the *B*-vinyl-9-BBN and the *gem*-dibora-9-BBN derivatives at the end of the reaction were then calculated with this particular set of parameters. The computer program was written on the basis of the formula of the Runge–Kutta method. Smaller d*t*'s were then substituted into eq 16 and 17, and the calculations were repeated until no significant change of the final concentrations was observed. For example, with $k_2/k_2' = 1.92$ of 1-hexyne, the calculated percentages of mono- and dihydroboration approached 49.4% and 25.3%, respectively. They are in very good agreement with the experimental results (eq 5). A plot of the correlation between k_2/k_2' and the percentage of monohydroboration obtained by this calculation procedure is given in Figure 1.

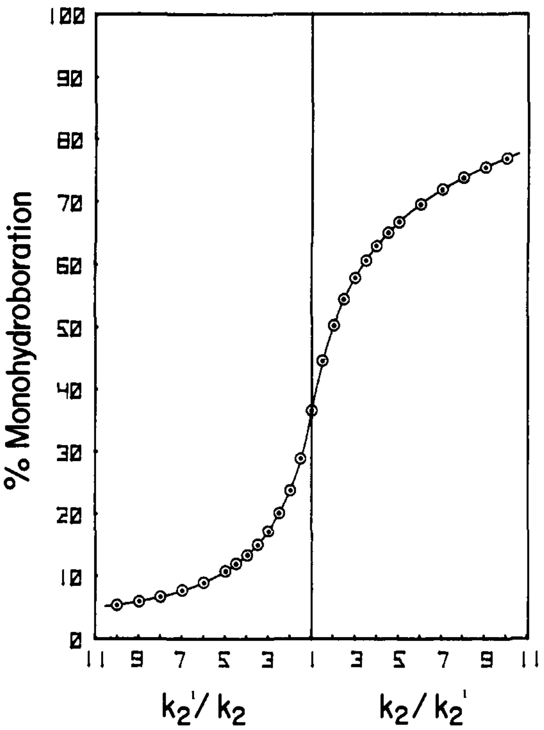

Figure 1. Correlation between ratio of the rate constants k_2 and k_2' and the percentage of monohydroboration.

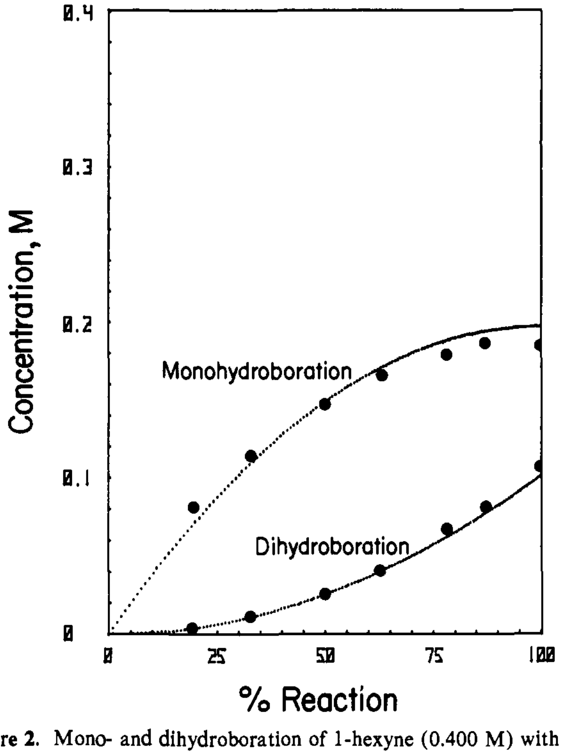

Figure 2. Mono- and dihydroboration of 1-hexyne (0.400 M) with $(9\text{-BBN})_2$ (0.200 M) in THF at 25 °C: (···) calculated data using $k_2/k_2' = 1.92$; (●) experimental data.

The calculated concentrations of the mono- and dihydroboration adducts during the entire reaction of 1-hexyne (0.400 M) with $(9\text{-BBN})_2$ (0.200 M) were also compared with the experimental data. Again, very good agreement was observed (Figure 2).

One of the applications of this calculation method is to predict the percentages of mono- and dihydroboration which will be observed when various excess amounts of an alkyne are used. For example, it was observed that at 25 °C 1-hexyne yields 46% monohydroboration and 27% dihydroboration when 1-hexyne was reacted with 1 equiv of 9-BBN in terms of the monomer. Therefore, k_2/k_2' of 1-hexyne is determined as 1.62 from Figure 1, in reasonable agreement with the above value from the com-

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[12] The chemical shift of the ^{11}B NMR spectrum of *B*-(*trans*-1-hexen-1-yl)-9-BBN in THF indicates that *B*-(*trans*-1-hexen-1-yl)-9-BBN is in rapid equilibrium with *B*-(*trans*-1-hexen-1-yl)-9-BBN·THF complex. Therefore, the relative reactivity of k_2' observed here may have been affected by the equilibrium of the reaction of *B*-(*trans*-1-hexen-1-yl)-9-BBN and THF to form the *B*-(*trans*-1-hexen-1-yl)-9-BBN·THF complex. A more detailed study will be given later.

[13] Kuo, S. S. "Computer Applications of Numerical Methods"; Addison-Wesley: Reading, MA, 1972.

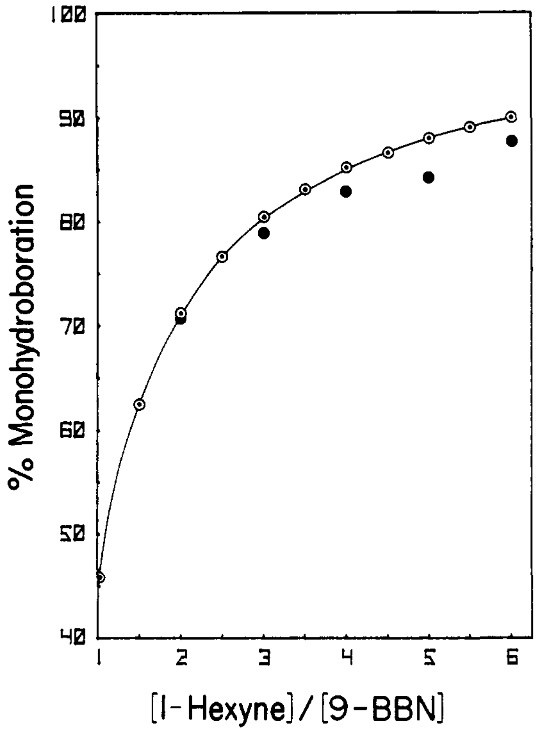

Figure 3. Percentage of monohydroboration of excess 1-hexyne with $(9\text{-BBN})_2$ in THF at 25 °C: (⊙) calculated data; (●) experimental data.

petitive determination. The relative values of k_2 and k_2' were then substituted into eq 16 and 17. The final concentrations of the mono- and dihydroboration adducts were then calculated when various amounts of 1-hexyne were used. A summary of the results of these calculations is given in Figure 3. They are in reasonable agreement with the experimental data.

It is clear from Figure 3 that 6 equiv of 1-hexyne is needed to achieve 90% of monohydroboration.[14] These calculations were then extended to other cases. A summary of the results is given in Figure 4. This information is very useful for synthetic applications. From Figures 1 and 4, one will be able to predict the amount of excess alkyne necessary to achieve a relatively clean monohydroboration in cases where a significant amount of dihydroboration was observed for the reaction of an alkyne with 1 equiv of 9-BBN in terms of the monomer.

Conclusion

The mechanism of the hydroboration of alkynes with $(9\text{-BBN})_2$ has been clearly established. It is very similar to that of the hydroboration of alkenes. The reaction proceeds through the prior dissociation of the 9-BBN dimer into the monomer, followed by the subsequent reactions of the monomer with the alkyne and its corresponding *B*-vinyl-9-BBN derivative.

The studies of the relative reactivities of alkynes indicated that the alkynes were not very reactive toward $(9\text{-BBN})_2$. This is in sharp contrast with that of the disiamylborane dimer and the dibromoborane–dimethyl sulfide complex. However, it allows one to take advantage of this broad range of reactivities of alkynes toward these hydroborating agents for synthetic applications. By properly choosing the hydroborating agent, one can selectively hydroborate a specific unsaturated carbon–carbon bond in the presence of others.

The relative reactivites of a terminal alkyne and its corresponding *B*-vinyl-9-BBN are very similar toward $(9\text{-BBN})_2$. Therefore, a large amount of dihydroboration adduct was observed. The difference is much larger for an internal alkyne, and thus much less dihydroboration adduct was observed. The numerical analysis of the dihydroboration phenomenon by the Runge–Kutta method with the help of a digital computer allows one to obtain much valuable information from the percentages of mono- and dihydoboration when an alkyne is reacted with 1 equiv of 9-BBN in terms of the monomer.

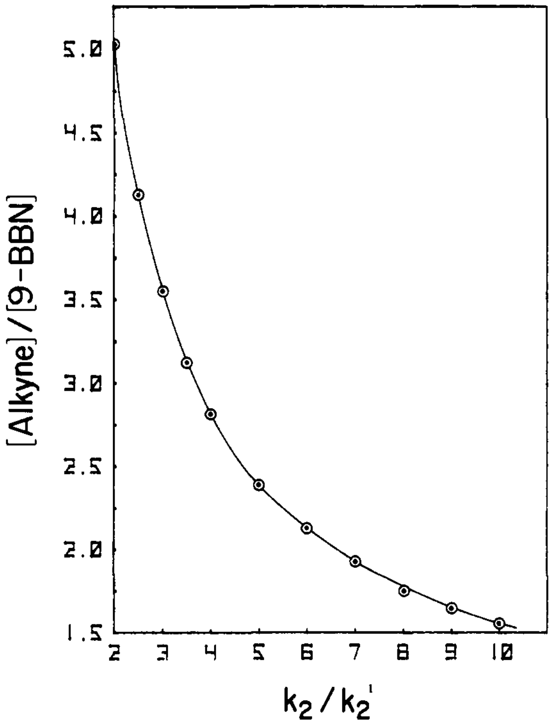

Figure 4. Equivalent of alkyne necessary to achieve 90% monohydroboration with various ratios of k_2/k_2'.

Experimental Section

General procedures for the manipulation of boron reagents have been outlined in Chapter 9 of ref 14. All glassware, syringes, and needles were oven dried at 140 °C for several hours before use. The glassware was assembled while hot and cooled under a stream of dry nitrogen. Syringes were assembled and fitted with needles while hot and then cooled as assembled units. They were flushed with nitrogen immediately before use. The quantitative analyses of the alkynes and alkenes were carried out on a Varian model 1200 GLC, equipped with a 0.25-in. injection port with an appropriate liner. The calculations and the plots of the kinetic data were carried out on a Hewlett-Packard 9820A calculator and a Hewlett-Packard 9862A calculator plotter, respectively.

Materials. The preparation of $(9\text{-BBN})_2$ and the purification of solvents were described elsewhere.[15] The alkanes (Phillips pure grade) employed as internal standards were used as received. The alkenes and alkynes were distilled under nitrogen from $LiAlH_4$ and $NaBH_4$, respectively, and then stored under nitrogen. The methanol (Mallinckrodt spectroquality) and ethanol (anhydrous reagent grade) employed as the quenching reagents were used as recieved.

Kinetics Procedure. The kinetics of the hydroboration of alkynes with $(9\text{-BBN})_2$ in various solvents at 25 °C were studied by two analytical methods. In the first method, a quantitative IR spectrometer was used to monitor the reaction of alkynes (0.20 M) with $(9\text{-BBN})_2$ (0.10 M). A detailed reaction procedure was given in ref 1c. In the second method, the reaction was followed by the quenching GLC method. A detailed reaction procedure was given in ref 1b. The quenching GLC method was used only to follow the reactions which do not exhibit a considerable amount of dihydroboration.

Relative Reactivities between Alkynes toward $(9\text{-BBN})_2$. The relative reactivities of alkynes toward $(9\text{-BBN})_2$ were studied by an indirect route. Typically, a more reactive alkene was chosen to compare with an alkyne. An example of the competitive hydroboration between an alkene and an alkyne toward $(9\text{-BBN})_2$ in THF at 25 °C is as follows: A 100-mL reaction flask was sucessively charged with 0.70 mL of 1-heptene (0.49 g, 5.0 mmol), 0.57 mL of 1-hexyne (0.41 g, 5.0 mmol), and 10 mL of

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(14) Our data indicate that the previous result[3] of using 2 equiv of 1-hexyne to achieve 94% of monohydroboration is probably too optimistic. However, the previous study was carried out at 0 °C. The effect of temperature on the percentage of monohydroboration is still yet to be carefully determined.

(15) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. "Organic Syntheses via Boranes"; Wiley-Interscience: New York, 1975.

THF solvent. *n*-Octane (0.6 mL) was added as an internal standard for GLC analyses. Several minute samples were removed and analyzed by GLC (a 0.25 in. × 6 in. 20% *N,N,N',N'*-tetrakis(2-hydroxyethyl)ethylenediamine (THEED) column to remove boranes, followed in series by a $^1/_8$ in. × 72 in. 30% adiponitrile column) for the initial flame ratios of 1-heptene/*n*-octane and 1-hexyne/*n*-octane. The samples were injected directly onto the THEED column, which was inserted into the injection port and maintained at 70–80 °C. The column oven containing the adiponitrile column was maintained at room temperature. The reaction was initiated by injecting 8.7 mL of $(9\text{-BBN})_2$ solution (0.29 M, 2.5 mmol) in THF into the stirred reaction mixture.

The reaction mixture was stirred 4 h at 25 °C to ensure complete reaction. A longer reaction time was needed for less reactive alkynes. A sample (0.5 mL) of the reaction mixture was withdrawn via a syringe and injected into a vial containing 0.5 mL of a 5% solution of glacial acetic acid in methanol. After standing for at least 1 h, the quenched sample was analyzed by GLC for the 1-heptene/*n*-octane and 1-hexyne/*n*-octane flame ratios. The relative reactivity between 1-heptene and 1-hexyne was calculated by using the Ingold–Shaw equation (eq 18)[16]

$$\frac{k_y}{k_x} = \frac{\log y_\infty - \log y_0}{\log x_\infty - \log x_0} \qquad (18)$$

in which y_0 = mmol of 1-heptene before reaction, y_∞ = mmol of 1-heptene after reaction, and x_0 and x_∞ = initial and final mmol of 1-hexyne. It was found that 1.24 mmol of 1-heptene and 4.07 mmol of 1-hexyne remained after the reaction. Consequently, the relative reactivity can be calculated as 6.8.

Several other pairs were studied to examine the influence of structure on the relative reactivity. These pairs include 1-decyne/1-octene, 3-methyl-1-butyne/1-hexene, cyclohexylethyne/1-octene, 3,3-dimethyl-1-butyne/1-heptene, phenylethyne/cyclooctene, 3-hexyne/2-methyl-2-butene, 4,4-dimethyl-2-pentyne/*cis*-3-hexene, and diphenylethyne/2,3-dimethyl-2-butene. The results are summarized in Table II.

Relative Rates (k_2/k_2') between Mono- and Dihydroboration of Alkynes with $(9\text{-BBN})_2$. The relative rates between mono- and dihydroboration of alkynes with $(9\text{-BBN})_2$ were also studied by an indirect route. An example of the relative reactivity between *B*-(*trans*-1-hexen-1-yl)-9-BBN and 3,3-dimethyl-1-butene is given as follows: To a 100-mL reaction flask was added 10 mL of THF, 0.45 mL (0.317 g) of *n*-octane (GLC internal standard), 1.18 mL (1.01 g at 0 °C, 5.0 mmol) of *B*-(*trans*-1-hexen-1-yl)-9-BBN, and 0.65 mL (0.42 g, 5.0 mmol) of 3,3-dimethyl-1-butene. *B*-(*trans*-1-Hexen-1-yl)-9-BBN was prepared as described elsewhere.[3] To the rapidly stirred reaction mixture maintained at 25 °C was added 8.7 mL of $(9\text{-BBN})_2$ solution (0.29 M, 2.5 mmol) in THF solvent. The reaction mixture was stirred 4 h at 25 °C to ensure complete reaction. A sample (0.5 mL) of the reaction mixture was withdrawn via a syringe and injected into a vial containing 0.5 mL of a 5% solution of glacial acetic acid in methanol. After standing for at least 1 h, the quenched sample was analyzed by GLC using the same conditions as just described. There were found 1.65 mmol of 3,3-dimethyl-1-butene and 3.44 mmol of 1-hexene [quenched product of *B*-(*trans*-1-hexen-1-yl)-9-BBN]. The relative reactivity between 3,3-dimethyl-1-butene and *B*-(*trans*-1-hexen-1-yl)-9-BBN was calculated by using the Ingold–Shaw equation (eq 18) as 2.96. Therefore, the relative reactivity (k_2/k_2') between 1-hexyne and *B*-(*trans*-1-hexen-1-yl)-9-BBN can be calculated as 2.96/1.54 = 1.92 (Table III).[1b]

The relative reactivity between *B*-(*cis*-3-hexen-3-yl)-9-BBN and 1-methylcyclohexene was also studied and found to be 0.302. Using this result, we calculated the relative reactivity (k_2/k_2') between 3-hexyne and *B*-(*cis*-3-hexen-3-yl)-9-BBN to be 193. These results are summarized in Table III.

Mono- and Dihydroboration of 1-Hexyne with 1 Equiv of 9-BBN in Terms of the Monomer. The amounts of mono- and dihydroboration of 1-hexyne during the reaction with 1 equiv of 9-BBN in terms of the monomer in THF at 25 °C were determined as follows: A 100-mL reaction flask was added with 2.63 mL of THF, 0.57 mL of 1-hexyne (0.41 g, 5.0 mmol), and 0.6 mL of *n*-octane (0.41 g, GLC internal standard). Several minute samples were removed and analyzed for the initial flame ratio of 1-hexyne/*n*-octane. The analytical conditions by GLC were the same as just described. The reaction was initiated by adding 8.7 mL of $(9\text{-BBN})_2$ solution (0.29 M, 2.5 mmol) in THF solvent to the rapidly stirred solution maintained at 25 °C. At appropriate intervals of time, aliquots (0.5 mL) were withdrawn and injected into vials containing 0.5 mL of a 5% solution of glacial acetic acid in methanol to quench the reaction. After standing for at least 1 h, the quenched sample was analyzed by GLC for the flame ratios of 1-hexyne/*n*-octane and 1-hexene/*n*-octane [1-hexene is the quenched product of the monohydroborated adduct, *B*-(*trans*-1-hexen-1-yl)-9-BBN].[3] The amounts of dihydroborated adduct were calculated according to eq 19. A summary of the results is given in Figure 2.

$$\text{mmol of } gem\text{-dibora-9-BBN} = (\text{initial mmol of 1-hexyne}) - (\text{residual mmol of 1-hexyne}) - (\text{mmol of 1-hexene}) \qquad (19)$$

Mono- and Dihydroboration of Excess Amounts of 1-Hexyne with $(9\text{-BBN})_2$. The percentages of mono- and dihydroboration of excess amounts of 1-hexyne with $(9\text{-BBN})_2$ in THF at 25 °C were also studied by the analytical procedure described above. After the reaction was complete, an aliquot (0.5 mL) of the reaction mixture was removed, quenched, and analyzed. The percentages of mono- and dihydroboration were then calculated.

Numerical Calculations of Mono- and Dihydroboration. The relationship between the percentages of mono- and dihydroboration and the relative reactivity (k_2/k_2') of an alkyne toward $(9\text{-BBN})_2$ was established by the numerical analysis. The differential eq 16 and 17 were integrated by the use of the Runge–Kutta method.[13] A computer program was written, and the calculations and the plots were carried out on a Hewlett-Packard 9820A calculator and Hewlett-Packard 9862A calculator plotter, respectively. For each set of parameters, the calculations were carried out to 99.9% completion of reaction. A detailed discussion of the calculations has been given in the text.

Registry No. $(9\text{-BBN})_2$, 70658-61-6; 1-hexene, 592-41-6; *cis*-3-hexene, 7642-09-3; 1-hexyne, 693-02-7; 1-decyne, 764-93-2; 3-methyl-1-butyne, 598-23-2; 3,3-dimethyl-1-butyne, 917-92-0; cyclohexylethyne, 931-48-6; phenylethyne, 536-74-3; 3-hexyne, 928-49-4; 4,4-dimethyl-2-pentyne, 999-78-0; diphenylethyne, 501-65-5; B-(trans-1-hexen-1-yl)-9-BBN, 69322-45-8; 3,3-dimethyl-1-butene, 558-37-2; B-(cis-3-hexen-3-yl)-9-BBN, 69322-51-6; 1-methylcyclohexene, 591-49-1; hexane-1,1-bis[9-BBN], 79919-22-5.

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[16] Ingold, C. K.; Shaw, F. R. *J. Chem. Soc.* **1927**, 2918–2926.

Total Synthesis of the Antitumor Antibiotic Streptonigrin[1]

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Abstract: Full details of the previously reported total synthesis of streptonigrin (**1**) are presented. The successful synthetic strategy outlined in Scheme I involves use of an imino Diels–Alder cycloaddition for construction of the pyridine C ring of **1** and a modified Friedlander synthesis for annulation of the AB quinoline quinone ring system.

A report which appeared approximately 20 years ago by workers at Chas. Pfizer and Co. described the isolation of a dark brown, crystalline compound named streptonigrin from cultures of *Streptomyces flocculus*.[3,4] Streptonigrin was of particular interest

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