(100), 166 (12), 151 (15), 110 (15); high-resolution mass spectrum calcd for $C_{38}H_{46}S_4$, m/e 630.2482; found, m/e 630.2465.

Cyclization of 1,1-Bis(phenylthio)-6,6-bis((*p*-*tert*-butylphenyl)thio)-hexane (19). To a solution of **19** (0.770 g, 1.22 mmol) and TMEDA (0.41 mL, 2.7 mmol) in 11.0 mL of anhydrous THF at 0 °C under argon was added methyllithium (1.65 mL, 1.55 M in diethyl ether, 2.56 mmol). The resulting solution was stirred for 6 h at 4 °C, at which time water was added and the resulting solution was extracted with ether. Concentration of the dried ($MgSO_4$) ether extract followed by purification by column chromatography (silica gel, eluted with 1% ethyl acetate in hexanes) afforded 0.46 g of an impure mixture of bicyclo[3.1.0]hexanes. Analysis of this crude mixture by RP-HPLC (5-μm octadecylsilyl column, 4.6 × 250 mm, eluted with 3% water in methanol, flow rate 1.0 mL/min) including co-injection experiments showed that the only bicyclic compounds formed were 6,6-bis(phenylthio)bicyclo[3.1.0]hexane (**4**), retention time 7.19 min, and 6,6-bis(*p*-*tert*-butylphenylthio)bicyclo-[3.1.0]hexane (**20**), retention time 17.8 min.

Detection of the Dianion (22) of 5,5-Bis(phenylthio)-1-pentanol. Quench with D_2O. *sec*-Butyllithium (0.75 mL, 1.1 M in cyclohexane, 0.82 mmol) was added to a solution of 5,5-bis(phenylthio)-1-pentanol (**21**) (0.119 g, 0.391 mmol) in 4.8 mL of anhydrous THF at −78 °C under argon. The resulting solution was stirred for 1 h at −78 °C at which time 2.0 mL of D_2O was added. The reaction mixture was extracted with ether, and the combined extracts were dried ($MgSO_4$), filtered, and concentrated. Purification by column chromatography (1 g of silica gel, eluted with hexanes followed by 20% ethyl acetate in hexanes) to remove a small amount of nonpolar impurities gave 0.080 g of a yellow oil whose NMR spectrum indicated that the recovered **21** was more than 93% deuterated at the thioacetal carbon atom: ^1H NMR (CCl_4, 90 MHz) δ 1.10–2.03 (m, 105, CH_2), 2.13 (br s, 16, OH), 3.53 (t, J = 7 Hz, 28, CH_2O), 4.37 (t, J = 6 Hz, 1, $CH(SPh)_2$), 7.13–7.67 (m, 139, Ph).

Cyclization of 5,5-Bis(phenylthio)-1-pentanol (21). *sec*-Butyllithium (4.10 mL, 1.09 M in cyclohexane, 4.47 mmol) was added to a solution of **21** (0.643 g, 2.11 mmol) and TMEDA (0.70 mL, 4.6 mmol) in 26.0 mL of anhydrous THF at −78 °C under argon. The resulting solution was stirred for 1 h at −78 °C and then at 4 °C for 20 h. The reaction was quenched by addition to 25.0 mL of a 10% aqueous NH_4Cl solution. The reaction mixture was concentrated by removal of the THF in vacuo and extracted with ether. Concentration of the dried ($MgSO_4$) extracts gave 0.672 g of crude products. Purification by column chromatography (60 g of silica gel, eluted with 10% ethyl acetate in hexanes followed by 20% ethyl acetate in hexanes) gave a first fraction of 0.0886 g (21.6%) of *cis*-2-(phenylthio)cyclopentanol: IR (film) 3650–3200 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.54–2.13 (m, 6 H, CH_2), 2.65 (br s, 1 H, OH) 3.41–3.49 (m, 1 H, C*H*SPh), 4.09 (t, J = 3.5 Hz, 1 H, CHO), 7.20–7.50 (m, 5 H, Ph); mass spectrum, (15 eV) m/e 194(M^+) (100), 166 (15), 110 (86), 85 (12), 84 (28), 67 (14); high-resolution mass spectrum calcd for $C_{11}H_{14}OS$, m/e 194.0765; found, m/e 194.0765. The slower moving component consisted of 0.056 g (13.8%) of *trans*-2-(phenylthio)cyclopentanol whose 300-MHz ^1H NMR was idential with that of an authentic sample:[29] IR (film) 3650–3125 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.54–1.88 and 2.00–2.31 (m, 7 H, CH_2 and OH), 3.36–3.43 (m, 1 H, C*H*SPh), 4.102 (m, 1 H, CHO), 7.16–7.43 (m, 5 H, Ph); mass spectrum, (15 eV) m/e 194 (M^+) (100), 166 (14), 110 (92), 84 (40), 83 (10), 67 (14); high-resolution mass spectrum calcd for $C_{11}H_{14}OS$, m/e 194.0765; found, m/e 194.0765.

Acknowledgment. We thank the National Science Foundation for general support of this work (CHE 7906651) and for providing the funds for purchase of the 300-MHz Bruker NMR instrument used in this study (CHE 7905185). We also thank Dr. Alvin Marcus for recording the mass spectra, Drs. Lin-Chen Yu and Fu-Tyan Lin for recording some of the NMR spectra, and Drs. James Matz and James J. Harrison for useful suggestions.

Hydroboration Kinetics. 6.[1] Hydroboration of Alkenes with 9-Borabicyclo[3.3.1]nonane Dimer and 9-Borabicyclo[3.3.1]nonane–Lewis Base Complexes in Various Solvents: An Interpretation of the Catalytic Effect of Ether Solvents on the Hydroboration Reaction

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Abstract: The hydroboration of alkenes with 9-borabicyclo[3.3.1]nonane dimer in noncomplexing solvents such as carbon tetrachloride, benzene, and cyclohexane and possible complexing solvents such as tetrahydrofuran, 2,5-dimethyltetrahydrofuran, and dimethyl sulfide and with 9-borabicyclo[3.3.1]nonane–amine complexes (pyridine, 2-methylpyridine, trimethylamine, and *N*-methylpiperidine) has been examined. These results provide an insight into the role of the complexing solvent on the hydroboration reaction. It is proposed that the complexing agent is not directly involved in the actual hydroboration step but provides an alternative lower energy pathway to monomeric boranes. This interpretation provides a reasonable explanation for the marked catalytic effect of ethers and weakly basic amines on the rate of hydroboration with diborane, a phenomenon previously not accounted for. This catalytic effect may well be a special example of a general phenomenon in reactions of associated organometallics.

The discovery of the enormous catalytic effect of ethers on the hydroboration of alkenes with diborane $(BH_3)_2$ more than two decades ago[3] marked the beginning of a rapid expansion of organoborane chemistry.[4] The reaction of an unhindered alkene with diborane is essentially instantaneous in ether solvents,[5] in sharp contrast with the extreme slowness of the reaction in the gas phase[6] and in hydrocarbon solvents (eq 1).[3c] Despite many

(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. (d) Wang, K. K.; Scouten, C. G.; Brown, H. C. *J. Am. Chem. Soc.* **1982**, *104*, 531–536. (e) Nelson, D. J.; Brown, H. C. *Ibid.* **1982**, *104*, 4907. (f) Nelson, D. J.; Brown, H. C.; Blue, C. D. *Ibid.* **1982**, *104*, 4913.

(2) Graduate research assistant on Grant CHE 76-20846 of the National Science Foundation.

(3) (a) Brown, H. C.; Subba Rao, B. C. *J. Am. Chem. Soc.* **1956**, *78*, 2582–2588. (b) *Ibid.* **1956**, *78*, 6594–6595. (c) *Ibid.* **1959**, *81*, 6428–6434.

(4) (a) Brown, H. C. "Hydroboration"; Benjamin: New York, 1962. (b) Brown, H. C. "Boranes in Organic Chemistry"; Cornell University Press: Ithaca, NY, 1972. (c) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. "Organic Syntheses via Boranes"; Wiley-Interscience: New York, 1975. (d) Cragg, G. M. L. "Organoboranes in Organic Synthesis"; Marcel Dekker: New York, 1973.

(5) Brown, H. C.; Subba Rao, B. C. *J. Org. Chem.* **1957**, *22*, 1136.

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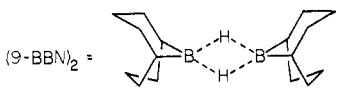
Table I. First-Order Rate Constants for the Hydroboration of Representative Alkenes with $(9\text{-BBN})_2$ in Various Solvents at 25 °C

	10^4k_1, s^{-1}					
alkene	CCl_4	cyclohexane	benzene	diethyl ether	THF	2,5-dimethyl-THF
1-hexene	1.54	1.45	2.05	2.83	14.2	2.29
2-methyl-1-pentene	1.53	1.51	1.99	2.81	14.3	2.48
3,3-dimethyl-1-butene	1.45	1.43	2.02	2.80	13.2	2.41
cyclopentene	1.52	1.52	2.06	2.77	10.8	2.28

attempts, the role of ether solvents in catalyzing the reaction is still not understood.

$$3(\text{alkene}) + 0.5(BH_3)_2 \xrightarrow[0°C,\ \text{fast}]{\text{ether solvent}} R_3B \qquad (1)$$

Recently we undertook a systematic investigation of the kinetics of hydroboration with 9-borabicyclo[3.3.1]nonane dimer (9-BBN)$_2$.[1] The reaction has been carried out in representative solvents



such as carbon tetrachloride, cyclohexane, benzene, diethyl ether, and tetrahydrofuran. The possibility for studying the reaction in this wide variety of solvents provided an opportunity to attain an understanding of the unusual effect of tetrahydrofuran (THF) and other ethers on the rates of the hydroboration reaction.

The earlier kinetic studies of the hydroboration of alkenes with $(9\text{-BBN})_2$ clearly established that the reaction proceeds through a prior dissociation of $(9\text{-BBN})_2$ into the monomer (eq 2) followed by reaction of the monomer with the alkene (eq 3).[1] For the more

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

$$9\text{-BBN} + \text{alkene} \xrightarrow{k_2} B\text{-alkyl-9-BBN} \qquad (3)$$

reactive alkenes such as 2-methyl-1-pentene, 1-hexene, 3,3-dimethyl-1-butene, and cyclopentene, the dissociation of $(9\text{-BBN})_2$ (eq 2) is the rate-determining step (Table I).

The first-order rate constant (k_1) for the dissociation of $(9\text{-BBN})_2$ (eq 2) is approximately 1.5×10^{-4} s^{-1} in both carbon tetrachloride and cyclohexane. It is slightly larger in benzene ($k_1 = 2.0 \times 10^{-4}$ s^{-1}) and larger still in diethyl ether ($k_1 = 2.8 \times 10^{-4}$ s^{-1}). A much larger increase, 10-fold, is observed in THF ($k_1 = 14.0 \times 10^{-4}$ s^{-1}).

Although the effect of ether solvents on the rate of hydroboration with $(9\text{-BBN})_2$ is not as dramatic as that for $(BH_3)_2$, it may still provide a valuable insight into the role of ether in the hydroboration reaction. Consequently, we undertook a systematic study to attain understanding of this phenomenon, one that has not been accounted for over more than two decades.

Results and Discussion

Mechanism and Hydroboration in THF and 2,5-Me$_2$THF. The first-order rate constant for the hydroboration of the more reactive alkenes with $(9\text{-BBN})_2$ in THF is approximately ten times larger than that in carbon tetrachloride, cyclohexane, or benzene (Table I). This increase has also been observed for other reactions of 9-BBN such as the hydroboration of alkynes,[1d] the reduction of aldehydes and ketones,[7] the protonolysis of alcohols and phenols,[7] and complex formation with amines.[7] It suggests that for some reason the dissociation of $(9\text{-BBN})_2$ into monomer must be faster in THF than in the other solvents examined.

It is possible to account for the faster rate in THF in terms of a direct attack of the THF molecule on the 9-BBN dimer, which breaks up the strong boron–hydrogen bridge bonds (eq 4). The

$$(9\text{-BBN})_2 + \text{THF} \rightleftharpoons 9\text{-BBN·THF} + 9\text{-BBN} \qquad (4)$$

$$9\text{-BBN} + \text{THF} \rightleftharpoons 9\text{-BBN·THF} \qquad (5)$$

Table II. First-Order Rate Constants for the Hydroboration of 2-Methyl-1-pentene with $(9\text{-BBN})_2$ in the Mixed Solvents of THF and CCl_4 at 25 °C

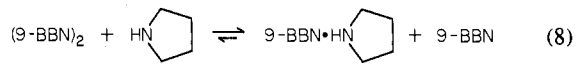
volume ratio CCl_4/THF	10^4k_1, s^{-1}
4/1	2.94
2/1	3.69
1/1	5.23
1/2	7.75
1/4	9.86

9-BBN monomer produced in eq 4 will be trapped by another THF molecule (eq 5). The 9-BBN·THF complex then reacts rapidly with the substrate, here proposed through the dissociation mechanism (eq 6 and 7).

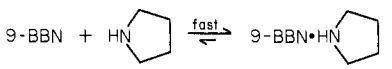
$$9\text{-BBN·THF} \rightleftharpoons 9\text{-BBN} + \text{THF} \qquad (6)$$

$$9\text{-BBN} + \text{substrate} \rightarrow \text{product} \qquad (7)$$

Because THF is the reaction solvent in large excess, the above reaction (eq 4–7) will exhibit pseudo-first-order kinetics, first-order in $(9\text{-BBN})_2$, for the reactive substrates. Consequently, the kinetic data cannot be used to distinguish between the direct attack reaction mechanism (eq 4–7) and the dissociation mechanism (eq 2 and 3). The direct attack mechanism is supported by our observation[7] that for certain unhindered amines such as pyrrolidine, the dominant reaction mechanism involves a direct attack of the amine on the 9-BBN dimer (eq 8 and 9). In this case, it is possible



(8)



(9)

to determine the reaction order with respect to the pyrrolidine. The data reveal that the reaction follows second-order kinetics, first-order in $(9\text{-BBN})_2$ and first-order in pyrrolidine, and the observed rate of the reaction is far faster than the rate of dissociation of $(9\text{-BBN})_2$ (eq 2).[7] Therefore, it is not unreasonable that the faster reaction of $(9\text{-BBN})_2$ with reactive alkenes in THF may proceed through a direct attack of THF on the 9-BBN dimer (eq 4).

In noncomplexing solvents such as carbon tetrachloride, cyclohexane, and benzene, this additional reaction pathway is not available; so the reaction proceeds only through the usual slow dissociation of dimer into monomer. In diethyl ether, the reaction rate is increased only slightly. This can be understood in terms of the much weaker Lewis basic characteristics of diethyl ether arising from its much larger steric requirements, reducing its ability to attack the 9-BBN dimer directly.

To test this effect of steric factors on the rate, we investigated the hydroboration of reactive alkenes with $(9\text{-BBN})_2$ in 2,5-dimethyltetrahydrofuran, 2,5-Me$_2$THF (cis and trans mixture), as solvent. The larger steric requirements of 2,5-dimethyltetrahydrofuran should make the direct attack mechanism (eq 4–7) less feasible. Indeed, the first-order rate of reaction in 2,5-dimethyltetrahydrofuran was much slower than that in THF, and the first-order rate constants (Table I) were very similar to those in the noncomplexing solvents. Apparently, dissociation of the dimer (eq 2 and 3) becomes the major reaction pathway.

We then examined the kinetics in mixtures of THF and carbon tetrachloride. It was observed that the rate of reaction is directly

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(7) Wang, K. K. Ph.D. Thesis, Purdue University, 1979.

proportional to the percentage of THF in the mixed solvent (Table II). This is consistent with the proposed interpretation involving a direct attack reaction pathway by THF.

The proposed direct attack mechanism for the reaction with $(9\text{-BBN})_2$ in THF solvent (eq 4–7) does not involve a direct reaction of 9-BBN·THF with the alkene. Instead, we propose a prior dissociation into free monomer (eq 6) prior to hydroboration (eq 7). According to our mechanism, the formation of 9-BBN·THF provides an alternative pathway to monomer with lower activation energy than the direct dissociation of the dimer. This alternative reaction pathway can also be used to account for the much faster hydroboration of alkenes with diborane in ether solvents.

Reaction with the 9-BBN·THF Complex. The direct attack mechanism requires that the 9-BBN·THF complex (eq 4 and 5) be a reaction intermediate. In fact, the experimental data support the conclusion that a significant amount of 9-BBN·THF complex exists in the THF solution.

In addition to the faster first-order reaction rate, the hydroboration in THF of 2-methyl-1-pentene, 1-hexene, 3,3-dimethyl-1-butene, and cyclopentene with $(9\text{-BBN})_2$ exhibits an additional unexpected characteristic. In this solvent there is an almost instantaneous initial disappearance of about 16% of the alkene for the hydroboration of these alkenes (0.200 M) with $(9\text{-BBN})_2$ (0.100 M). The reaction then exhibits normal first-order kinetics. No such rapid initial reaction was observed with the other solvents examined. This rapid initial reaction is attributed to the formation of an equilibrium concentration of 9-BBN·THF complex, which reacts very rapidly with the added alkene (eq 6 and 7). On this basis, the equilibrium constant for the reaction of $(9\text{-BBN})_2$ with THF to form 9-BBN·THF complex (eq 10) is readily calculated (eq 11). According to this equilibrium constant, the percentage of $(9\text{-BBN})_2$ that exists as the 9-BBN·THF complex should increase to 40% for a 0.0100 M solution of $(9\text{-BBN})_2$ in THF. Indeed, at this concentration, an initial rapid disappearance of 40% of 2-methyl-1-pentene (0.0200 M) is observed.

$$(9\text{-BBN})_2 + 2\text{THF} \rightleftharpoons 2(9\text{-BBN·THF}) \qquad (10)$$

$$K = \frac{[9\text{-BBN·THF}]^2}{[(9\text{-BBN})_2][\text{THF}]^2} = \frac{(0.100 \times 2 \times 0.16)^2}{(0.100 \times 0.84)(12.3)^2} = 8.05 \times 10^{-5}\ \text{M}^{-1} \qquad (11)$$

The presence of the 9-BBN·THF complex is further supported by the ^{11}B NMR spectrum.[8] The ^{11}B NMR spectrum of 9-BBN in THF shows two peaks. The much larger singlet peak at 27.7 ppm (external standard $BF_3{\cdot}OEt_2$, δ = 0.00 ppm) is due to the 9-BBN dimer. The doublet peak at 15.2 and 12.3 ppm is attributed to the 9-BBN·THF complex. The existence of the peak as a doublet suggests that a hydrogen atom is directly attached to the boron atom. The proton-decoupled ^{11}B NMR spectrum causes the doublet to collapse into a singlet at 13.8 ppm. The upfield chemical shift of the doublet indicates that the 9-BBN monomer is complexed with a THF molecule.[9]

The infrared spectrum of 9-BBN in THF shows a small peak at 2300 cm^{-1}, the absorption region of the boron–hydrogen terminal bond,[9] in addition to the strong absorption of boron–hydrogen bridge bonds at 1570 cm^{-1}. This small peak at 2300 cm^{-1} is also attributed to the presence of the 9-BBN·THF complex.

The absorption peak at 2300 cm^{-1} was monitored with a quantitative infrared spectrometer. To a solution of 25.0 mL of 0.100 M $(9\text{-BBN})_2$ (2.5 mmol) in THF was added 0.21 g of 2-methyl-1-pentene (0.31 mL, 2.5 mmol, half the stoichiometric amount). The peak at 2300 cm^{-1} disappeared immediately. However, after about 5 min this peak began to reappear, reaching its maximum absorbance (about 61% of the initial absorbance) within 15 min. An additional 0.105 g of 2-methyl-1-pentene (0.155 mL, 1.25 mmol) was then added to the reaction flask. This peak again disappeared immediately, reappearing about 5 min later, reaching its maximum absorbance (37% of the initial absorbance) within 15 min.

The rapid initial disappearance of the peak is attributed to the very fast reaction between the 9-BBN·THF complex and 2-methyl-1-pentene. After 5 min, all of the alkene would have been reacted and the equilibrium between $(9\text{-BBN})_2$ and 9-BBN·THF complex would begin to be reestablished. Therefore, the peak reappears. The reappearance of the peak strongly supports the existence of a mobile equilibrium between $(9\text{-BBN})_2$ and the 9-BBN·THF complex.

The 5-min period necessary for the remaining 1.7 mmol of 2-methyl-1-pentene to react with $(9\text{-BBN})_2$ is in good agreement with our previous observation that the half-life for the first-order reaction with $(9\text{-BBN})_2$ in THF is about 8 min ($k_1 = 14.0 \times 10^{-4}$ s^{-1}). The maximum absorbances of the peak that reappears are also in good agreement with that calculated from the equilibrium constant (eq 11).

Mechanism of the Reaction of the 9-BBN·THF Complex with Alkenes. Two alternative mechanisms for the reaction of the 9-BBN·THF complex with the reactive alkenes must be considered. One possibility is that the reaction proceeds through a direct attack of the 9-BBN·THF complex on the alkene (eq 12). The second possibility is that the 9-BBN·THF complex undergoes prior dissociation to the free 9-BBN monomer (eq 13), followed by a fast reaction of the monomer with the alkene (eq 14).

$$9\text{-BBN·THF} + \text{alkene} \rightarrow B\text{-alkyl-9-BBN} + \text{THF} \qquad (12)$$

$$9\text{-BBN·THF} \underset{k_{-1'}}{\overset{k_{1'}}{\rightleftharpoons}} 9\text{-BBN} + \text{THF} \qquad (13)$$

$$9\text{-BBN} + \text{alkene} \rightarrow B\text{-alkyl-9-BBN} \qquad (14)$$

It was established that the relative reactivities of several alkene pairs toward 9-BBN in carbon tetrachloride are the same as the corresponding reactivities of the same alkene pairs toward 9-BBN in tetrahydrofuran (Table III). This supports the conclusion that the actual hydroborating agent must be the same in both systems. In carbon tetrachloride, we have established that the actual hydroborating agent is the free 9-BBN monomer.[1] Consequently, we conclude that the actual hydroborating agent in tetrahydrofuran solution must also be the free 9-BBN monomer.

This raises an interesting problem. The fact is that the 16% of 9-BBN·THF complex present in 0.100 M $(9\text{-BBN})_2$ in THF reacts with the reactive alkenes far faster than the dimer itself. This requires that the dissociation of the complex into monomer must proceed at a rate far greater than the rate of dissociation of dimer into monomer.

Hydroboration of Alkenes with $(9\text{-BBN})_2$ in Dimethyl Sulfide. In dimethyl sulfide solvent, the amount of 9-BBN that exists as the monomeric complex, 9-BBN·SMe_2, is considerably greater than the amount that exists as the complex in THF, 9-BBN·THF, under the same conditions (25 °C, pure solvent).[7,8c] Indeed, the kinetic data for a 0.100 F solution of 9-BBN in Me_2S indicate the presence of 61% of a highly reactive species, presumably 9-BBN·SMe_2. With an expression similar to that of eq 11, the equilibrium constant is calculated to be 2.1×10^{-3} M^{-1}, as compared to the value of 8.05×10^{-5} M^{-1} for 9-BBN in THF.

The addition of 0.200 M 2-methyl-1-pentene to a solution of 0.100 M $(9\text{-BBN})_2$ in Me_2S results in an almost instantaneous

Table III. Relative Reactivities of Alkenes toward $(9\text{-BBN})_2$ in Carbon Tetrachloride and Tetrahydrofuran at 25 °C

alkene pair	relative reactivity	
	CCl_4	THF
1-hexene/3,3-dimethyl-1-butene	4.3	4.2
cyclopentene/3,3-dimethyl-1-butene	0.31	0.31
2-methyl-2-butene/1-methylcyclopentene	0.61	0.57
cis-3-hexene/1-methylcyclopentene	0.36	0.37
2-methyl-2-butene/*cis*-4,4-dimethyl-2-pentene	2.2	2.3

(8) (a) Reference 7, p 164. (b) Contreras, R.; Wrackmeyer, B. *Z. Naturforsch., B: Anorg. Chem., Org. Chem.* **1980**, *35b*, 1236–1240. (c) Soderquist, J. A.; Brown, H. C. *J. Org. Chem.* **1981**, *46*, 4599–4600.

(9) Negishi, E.; Katz, J.-J.; Brown, H. C. *J. Am. Chem. Soc.* **1972**, *94*, 4025–4027.

Table IV. First-Order Rate Constants for the Reaction of 2-Methyl-1-pentene, Hexanal, and Cyclohexanone with $(9\text{-BBN})_2$ in Dimethyl Sulfide at 25 °C

substrate	rate constant, $10^4 k_1$, s^{-1}
2-methyl-1-pentene	6.06
hexanal	6.03
cyclohexanone	6.00

disappearance of 61% of the alkene, followed by the usual slower first-order reaction. We attribute this fast initial uptake of the alkene to a very fast reaction with 61% of the 9-BBN·SMe_2 present in the solution.

We tested this interpretation by examining the behavior of a more concentrated solution of $(9\text{-BBN})_2$ in Me_2S. The above equilibrium constant indicates that in a solution that is 0.200 M in $(9\text{-BBN})_2$, the amount of 9-BBN·SMe_2 should be 49%. Indeed, the addition of 0.400 M 2-methyl-1-pentene to this solution resulted in the almost instantaneous disappearance of 49% of the alkene.

It should be pointed out that the presence of a highly reactive species, which we attribute to the presence of 9-BBN·SMe_2, can also be detected by an unusually fast reaction of the 9-BBN·SMe_2 present with hexanal[7] and with cyclohexanone[7] (Table IV). We are faced with the same question. How can we account for the remarkably higher reactivity of 9-BBN·SMe_2, as compared to that of the dimer? Again we will defer discussion of this point to a later section.

Following the initial fast stage, the reaction proceeds, exhibiting simple first-order kinetics, first-order in $(9\text{-BBN})_2$. Apparently the rate of the dissociation of $(9\text{-BBN})_2$ into free 9-BBN now becomes the rate-determining step. These first-order rate constants are larger than those in noncomplexing solvents (Table I) but smaller than those in THF. Presumably, as previously discussed for THF (eq 4), Me_2S can also assist by dissociating the dimer into the more reactive complex, although less effectively than THF.

The hydroboration of a less reactive alkene, cyclopentene, with the 9-BBN·SMe_2 complex is slower. It required approximately 2.5 min for the disappearance of 50% of the 9-BBN·SMe_2 complex in the reaction of 0.400 M cyclopentene with 0.200 M $(9\text{-BBN})_2$. This is attributed to the lower reactivity of cyclopentene toward the dissociated 9-BBN monomer. Indeed, our competitive study described previously established that the reactivity of 2-methyl-1-pentene to 9-BBN is 27 times greater than that of cyclopentene.[10] For reaction with such relatively sluggish alkenes, recombination of the 9-BBN monomer with Me_2S can become competitive with the reaction with alkene.

Hydroboration of Alkenes with 9-BBN·Amine Complexes. The reaction of pyridine with $(9\text{-BBN})_2$ proceeds to essential completion at 25.0 °C (eq 15).[10] In this case the reaction of the

$$(9\text{-BBN})_2 + 2\text{Py} \rightleftharpoons 2(9\text{-BBN·Py}) \qquad (15)$$

complex with reactive alkenes at 25.0 °C is quite slow. The difference between the behavior of this addition compound in its reaction with alkenes and that exhibited by 9-BBN·THF and 9-BBN·SMe_2 is attributed to the far higher stability of 9-BBN·Py, resulting in a very low rate of dissociation into monomer.

The reaction of trimethylamine with $(9\text{-BBN})_2$ also proceeds to essential completion at 25.0 °C (eq 16).[10] However, this

$$(9\text{-BBN})_2 + 2\text{NMe}_3 \rightleftharpoons 2(9\text{-BBN·NMe}_3) \qquad (16)$$

addition compound reacts with reactive alkenes at a modest rate (~50% in 1 h at 25.0 °C, 0.300 M in each component) (Figure 1). Apparently, dissociation into monomer proceeds at a modest rate, far slower than the rates of the 9-BBN·THF and 9-BBN·SMe_2 complexes.

The dissociation mechanism for the reaction of 9-BBN·NMe_3 was tested by studying the kinetic effect of excess trimethylamine on the rate of hydroboration of 2-methyl-1-pentene. Indeed, the rate was considerably decreased by adding 50% excess NMe_3 to the reaction mixture (Figure 1). Evidently the excess NMe_3 decreases the equilibrium concentration of the reactive monomer, decreasing the observed rate of the hydroboration reaction. Had the reaction involved a direct attack of the addition compound on the alkene (similar to eq 12), the reaction rate should not have been affected by the presence of excess NMe_3.

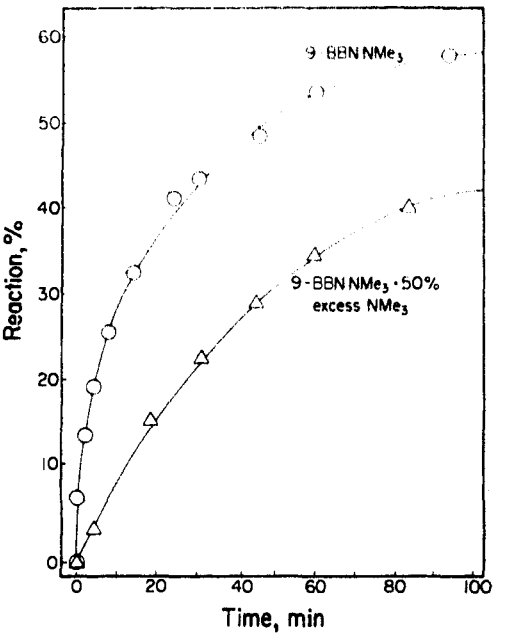


Figure 1. Rate data for the hydroboration of 2-methyl-1-pentene (0.300 M) with 9-BBN·NMe_3 complex (0.300 M) in THF at 25 °C in the presence and absence of excess trimethylamine.

It was observed previously that an increase in the steric requirements of the amine or a decrease in the base strength of the amine decreases the stability of the 9-BBN·amine complexes.[11] Accordingly, we sought for bases that would largely dissociate $(9\text{-BBN})_2$ but would be less stable than the 9-BBN·Py and 9-BBN·NMe_3 derivatives. In accordance with our interpretation, these adducts should exhibit fast rates of hydroboration with 2-methyl-1-pentene and similar reactive alkenes.

2-Methylpyridine (0.300 M) reacts with $(9\text{-BBN})_2$ in THF (0.150 M) to go to essentially complete formation of the addition compound (eq 17). In contrast to the Py derivative, this 2-MePy

$$(9\text{-BBN})_2 + 2(2\text{-MePy}) \rightleftharpoons 2(9\text{-BBN·2-MePy}) \qquad (17)$$

derivative reveals a very fast reaction with 2-methyl-1-pentene, the reaction being approximately 50% complete in 2 min at 25.0 °C (Figure 2). We interpret this greater reactivity to a fast rate of dissociation of the addition compound into 9-BBN monomer brought about by the large steric effect of the 2-methyl substituent.[11]

N-Methylpiperidine forms a less stable adduct, the formation of complex at 25.0 °C for a 0.300 M solution in THF being 86% complete. The reaction of this complex with 2-methyl-1-pentene was even faster than that of the 2-MePy complex (Figure 2).

Finally, we examined the 1:1 and 2:1 complexes of *N,N,N',N'*-tetramethylethylenediamine with 9-BBN.[10] Both react at reasonable rates, with the rate for the less stable 2:1 complex exceeding that for the 1:1 complex (Figure 2).

As was pointed out earlier, we are faced with this question. Our results require that the fast reactions of these addition compounds proceed through dissociation into the monomer. How can we explain why an addition compound, readily formed from the dimer by reaction with a suitable base, dissociates into monomer faster than the dimer itself?

(10) Brown, H. C.; Kulkarni, S. U. *Inorg. Chem.* **1977**, *16*, 3090–3094.

(11) (a) Brown, H. C.; Wang, K. K. *Recl. Trav. Chim. Pays-Bas* **1979**, *98*, 117–120. (b) Brown, H. C.; Wang, K. K. *J. Org. Chem.* **1980**, *45*, 1748–1753.

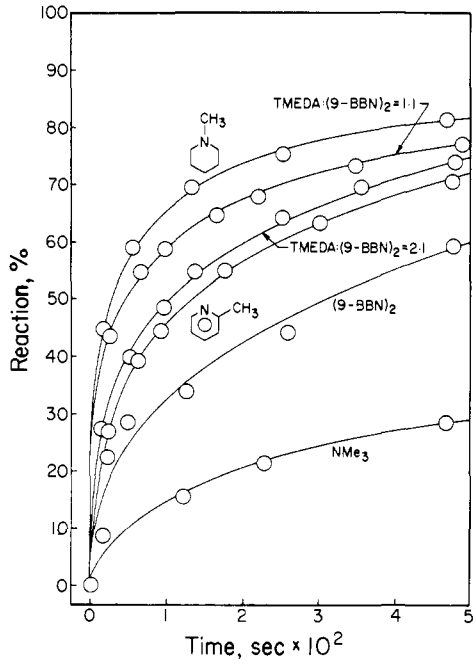


Figure 2. Rate data for the reaction of 2-methyl-1-pentene (0.300 M) with various 9-BBN·amine complexes (0.300 M) in THF at 25 °C.

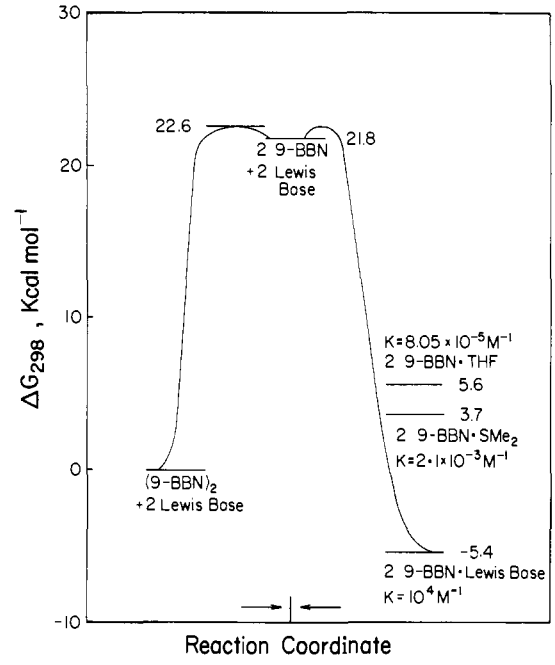


Figure 3. Free energy diagram for the 9-BBN system.

Theoretical Basis for the Enhanced Reaction of Certain 9-BBN·Lewis Base Complexes. The discovery that certain 9-BBN·Lewis base complexes are more reactive toward 2-methyl-1-pentene than $(9\text{-BBN})_2$ itself is of great interest. One question necessary arises. How can these 9-BBN·Lewis base complexes be thermodynamically more stable but kinetically more reactive than the dimer? The answer to this question has many theoretical implications and could bring about an understanding of the marked catalytic effect of ethers on the rate of diborane hydroboration.

As pointed out earlier, the identical relative reactivity data that we observed for hydroboration of pairs of alkenes with 9-BBN in carbon tetrachloride and in THF support the conclusion that the reactive intermediate must be the same in both systems. We identified that intermediate as the free 9-BBN monomer. The repression by excess NMe_3 of the rate of reaction of 9-BBN·NMe_3 with alkenes also points to a reaction that proceeds via dissociation of the addition compound into free 9-BBN monomer. Because both the 9-BBN·Lewis base complexes and the 9-BBN dimer react with alkenes through the dissociation mechanism, the faster reaction rates of these 9-BBN·Lewis base complexes toward 2-methyl-1-pentene indicate that they must have faster rates of dissociation into the monomer than does the dimer.

The relationship between the rate of dissociation of the 9-BBN·Lewis base complex (eq 18) and that of the 9-BBN dimer (eq 19) is given as follows:

$$\text{9-BBN·Lewis base} \underset{k_{-1}'}{\overset{k_1'}{\rightleftharpoons}} \text{9-BBN + Lewis base} \quad (18)$$

$$(\text{9-BBN})_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} 2(\text{9-BBN}) \quad (19)$$

At equilibrium, eq 20 can be derived by eliminating the term for 9-BBN monomer. This is the equilibrium equation for the overall process (eq 21).

$$(k_1/k_{-1})/(k_1'/k_{-1}')^2 = \frac{[\text{9-BBN·Lewis base}]^2}{[(\text{9-BBN})_2][\text{Lewis base}]^2} = K \quad (20)$$

$$(\text{9-BBN})_2 + 2(\text{Lewis base}) \rightleftharpoons 2(\text{9-BBN·Lewis base}) \quad (21)$$

For the formation of a moderately stable complex, reaction >90% of the addition adducts for solutions 0.200 M $(9\text{-BBN})_2$ and 0.400 M Lewis bases, the equilibrium constant may be calculated to be $K = 10^4$ M^{-1} (eq 11 and 20). By substituting $K = 10^4$ M^{-1} into eq 20, we arrive at a relationship between k_1' and k_{-1}' for such relatively stable addition compounds (eq 22).

$$k_1'/k_{-1}' = 10^{-2}(k_1/k_{-1})^{1/2} \quad (22)$$

$\Delta G^{\ddagger}_{298}$ for the dissociation of $(9\text{-BBN})_2$ can be calculated from the known rate constant k_1 by using the Eyring equation.[12] For $k_1 = 1.54 \times 10^{-4}$ s^{-1}, the observed rate constant for reactions in noncomplexing solvents, $\Delta G^{\ddagger}_{298}$, can be calculated to be 22.6 kcal mol^{-1}. Therefore, the ground-state energy difference between $(9\text{-BBN})_2$ and two uncomplexed 9-BBN monomers must be slightly smaller than 22.6 kcal mol^{-1}. For simplicity, it is assumed to be 21.8 kcal mol^{-1} (see Figure 3), which leads to a value for k_1/k_{-1} of 10^{-16}. (The precise value estimated for k_1/k_{-1} is unimportant as long as it is small enough to give a much larger k_1'/k_{-1}' value when it is substituted into eq 22).

Substituting $k_1/k_{-1} = 10^{-16}$ into eq 22, one finds that the ratio between k_1' and k_{-1}' becomes 10^{-10}. Therefore, ΔG°_{298} for eq 18 is only 13.6 kcal mol^{-1}. However, ΔG°_{298} for eq 19 is 21.8 kcal mol^{-1}. The $\Delta\Delta G^{\circ}_{298}$ is 8.2 kcal mol^{-1}—no small factor—for the difference in the ground-state energies of these two different processes (dimer → 2 monomer; 9-BBN·Lewis base complex → monomer + Lewis base). Although one should use $\Delta G^{\ddagger}_{298}$ to compare the rates of the reaction, the much smaller difference in ΔG°_{298} for eq 18 would certainly contribute greatly to the faster rate of dissociation of the complex relative to the rate of dissociation of the dimer.

The free energy diagram for the 9-BBN system is given in Figure 3. At first sight, it might appear that the rate of dissociation of the complex to monomer must be slower than the rate of dissociation of dimer into monomer, since the complex lies at a considerably lower energy level. For the particular example here considered, with $K = 10^4$ M^{-1}, the complex would be lower than the dimer in energy by 5.4 kcal mol^{-1}, leading apparently to a dissociation energy of 27.2 kcal mol^{-1} (21.8 + 5.4 kcal mol^{-1}). This appears to be considerably larger than the difference in energy between $(9\text{-BBN})_2$ and the monomer, 2 9-BBN: 21.8 kcal mol^{-1}.

The apparent anomaly is resolved by noting that 27.2 kcal mol^{-1} is really the difference in energy between two 9-BBN·Lewis base complexes and two 9-BBN monomers plus two free Lewis bases. Therefore, the difference in the ground-state energies for dissociation of the 9-BBN·Lewis base complex into its components is really only one-half this quantity, 13.6 kcal mol^{-1}. This is also

(12) (a) Eyring, H. *J. Chem. Phys.* **1935**, *3*, 107–116. (b) Glasstone, S.; Laidler, K. J.; Eyring, H. "The Theory of Rate Processes"; McGraw Hill: New York, 1941.

the number that was calculated above directly from eq 22.

It is clear from this treatment that a strong Lewis base such as pyridine with an equilibrium constant much larger than 10^4, will result in a rate of dissociation of the 9-BBN·Lewis base becoming slower than that of $(9\text{-BBN})_2$. In addition, the alkene will be less able to compete with the stronger Lewis base for the dissociated free 9-BBN monomer. Such addition compounds will exhibit a slow hydroboration rate, as observed.

On the other hand, for certain Lewis bases such as 2-methylpyridine, the equilibrium constants are just large enough for the 9-BBN to exist essentially completely as the 9-BBN·Lewis base complex, greater than 98% for 9-BBN·2-MePy at the concentration studied but not prohibitively large so that the complex can dissociate into monomer faster than $(9\text{-BBN})_2$, as described above. For THF and Me_2S, the equilibrium constants are still smaller, so that dimer and addition compounds exist competitively in solution. The smaller equilibrium constants predict an even faster rate of dissociation of the complexes into monomer, in accordance with the very fast initial rates that were observed for these solutions.

Qualitatively speaking, this rate enhancement by certain Lewis bases comes about because only one chemical bond of the 9-BBN·Lewis base complexes needs to be broken in the course of the dissociation of the 9-BBN·Lewis base complexes into the reactive monomeric species, as compared to the requirement for the simultaneous breaking of two boron–hydrogen bridge bonds in the dissociation of $(9\text{-BBN})_2$ into its reactive monomer. In terms of the thermochemistry of the system, one molecule of $(9\text{-BBN})_2$, in reacting with a relatively strong Lewis base, will form two donor–acceptor bonds, producing two molecules of the 9-BBN·Lewis base complex. The combined free energy of the two 9-BBN·Lewis base complexes makes them more stable than uncombined $(9\text{-BBN})_2$ and two free Lewis bases. If we had to rupture both donor–acceptor bonds in the product simultaneously to form monomer, such complexes would always be less reactive than the dimer itself. It is the requirement that only one of these stronger donor–acceptor bonds needs be broken at a time that makes it possible for the formation of monomer from the addition compound, over certain ranges of k, be faster than its formation from dimer, where two boron–hydrogen bonds must be broken simultaneously.

Interpretation of the Enormous Catalytic Effect of Ether Solvents and Weak Lewis Bases on Hydroboration with Diborane. In the gas phase[6] and in hydrocarbon solvents,[3c] diborane reacts exceedingly slowly with alkenes. The energy of dissociation of diborane into two borane fragments (eq 23) has been estimated to be about 35 kcal mol^{-1}.[13] If such hydroboration reactions proceed through the dissociation mechanism (eq 23 and 24), it is not surprising that the rates are so slow.

$$(BH_3)_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} 2BH_3 \qquad (23)$$

$$BH_3 + 3(\text{alkene}) \rightarrow R_3B \qquad (24)$$

These hydroboration reactions involving diborane are catalyzed enormously by ether solvents[5] and weak Lewis bases.[14] The question we set ourselves was whether the interpretation we have presented for the enhanced reaction rates observed for the reaction of reactive alkenes with $(9\text{-BBN})_2$ in THF solvent and with certain 9-BBN·Lewis base complexes could be extended to account for these enormous catalytic effects afforded the diborane reaction by ether solvents and weak Lewis bases.

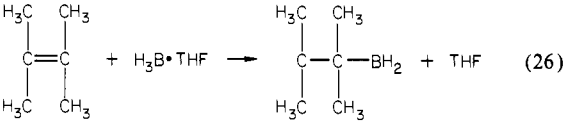
Diborane exists in THF solution predominantly as the H_3B·THF complex.[15] In this solvent, the hydroboration of most unhindered alkenes is enormously fast, almost instantaneous. We propose to explain this very fast rate in the same way we accounted for the enhanced rates of certain 9-BBN·Lewis base complexes, namely, a dissociation of the H_3B·THF complex into monomeric borane (eq 25) that is far faster than the dissociation of diborane

$$H_3B\cdot THF \underset{k_{-1}'}{\overset{k_1'}{\rightleftharpoons}} H_3B + THF \qquad (25)$$

itself into monomer (eq 23). An energy diagram similar to Figure 3 would apply to this system. In other words, even though 2-(H_3B·THF) is thermodynamically more stable than diborane plus 2THF, the dissociation to borane, with the need to break individual bonds in the complex, would be faster than the breaking of both boron–hydrogen bonds in diborane itself.

The reaction of H_3B·THF with alkenes has been studied previously, with conflicting conclusions. With the help of a flow method and spectroscopic observation, Klein and co-workers examined the kinetics of the fast reaction of H_3B·THF with styrenes.[16] They concluded that the reaction was second order, first order in H_3B·THF and first order in styrene. They made the important observation that the reaction of an aged solution of *m*-methoxystyrene, presumably contaminated by some impurity (possibly peroxide), exhibits an induction period attributed to the depletion of a reactive intermediate, either dissociated free H_3B monomer or the associated dimer, by the impurity present. In other words, there was no direct reaction of H_3B·THF with the styrene. Only after the impurity had all reacted was styrene hydroborated.

Pasto and co-workers examined the reaction of 2,3-dimethyl-2-butene with H_2BCl·THF in THF[17] as well as the reaction of the same alkene with H_3B·THF.[18] In both cases the reactions exhibited second-order kinetics, first order in both 2,3-dimethyl-2-butene and first order in the borane complex. From the observed entropies of activation, they deduced that the reactions must proceed through a direct reaction of the alkene with the borane complex (eq 26).



(26)

Over the years arguments based on entropies of activation have not provided a satisfactory basis for decisions as to reaction mechanisms. We believe that both Klein's observation of an induction period and our observations on the 9-BBN system argue strongly for the dissociation mechanism. We are studying directive effects in hydroboration by representative borane complexes in an effort to obtain definite evidence on this question.

The enormous catalytic effect of THF on the rate of hydroboration of alkenes with diborane can be regarded as a special example of a general phenomenon. A Lewis base capable of forming a weak complex with BH_3 should also facilitate the reaction. Indeed, diborane forms a weak complex with dimethyl sulfide, H_3B·SMe_2.[19] This product can be isolated as a 1:1 complex; so it is somewhat more stable than H_3B·THF, which can be prepared only as a dilute solution in THF. Hydroboration with H_3B·SMe_2 is quite fast,[20] although somewhat slower than is the case with H_3B·THF,[21] in accordance with the relative stabilities of the two complexes.

Amine complexes such as H_3B·Py and H_3B·NMe_3 are quite stable. Hydroboration of alkenes with these addition compounds does not occur at 25.0 °C. However, the introduction of increased steric effects into the amine, as in the case of 2,6-lutidine (eq 27),

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(17) Pasto, D. J.; Kang, S.-Z. *J. Am. Chem. Soc.* **1968**, *90*, 3797–3800.
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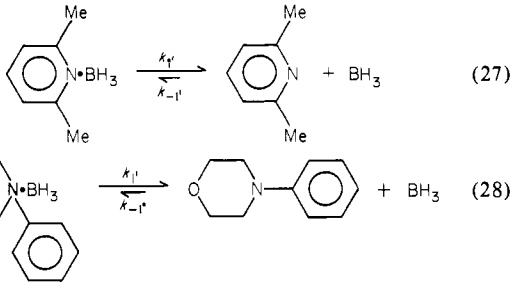
(20) Braun, L. M.; Braun, R. A.; Crissman, H. R.; Opperman, M.; Adams, R. M. *J. Org. Chem.* **1971**, *36*, 2388–2389.
(21) Brown, H. C.; Mandal, A. K.; Kulkarni, S. U. *J. Org. Chem.* **1977**, *42*, 1392–1398.

and of decreased electron availability, as in *N*-phenylmorpholine (eq 28), decrease the stability of the complex and dramatically increase the hydroboration rate.[14,22]



(27)

(28)

In both diglyme (DG) and ethyl ether (EE), diborane exists mainly as the dimer.[15a] However, much faster hydroboration rates involving diborane are also observed in these solvents.[3] Can we account for the very fast hydroboration rates observed in these solvents?

It is possible to account for them by postulating the fast formation of a small equilibrium concentration of borane–ether in these systems, followed by the same mechanism used to explain the faster first-order reaction rate for the reaction of reactive alkenes with $(9\text{-BBN})_2$ in THF. It was proposed that in THF solvent the THF molecule is capable of a direct attack on the 9-BBN dimer, breaking the strong boron–hydrogen bridge bonds to form the 9-BBN·THF complex capable of dissociating rapidly into the reactive monomer (eq 4 and 5). Diglyme or ethyl ether molecules must also be capable of attacking diborane directly, breaking up the strong boron–hydrogen bridge bonds to form rapidly a small equilibrium concentration of the corresponding H_3B·DG or H_3B·EE complexes. These complexes should be able to dissociate into the reactive free H_3B monomer even more rapidly than the relatively stable H_3B·THF complex.

In this way the interpretation we have advanced to account for the behavior of $(9\text{-BBN})_2$ in various solvents and complexed with various weak Lewis bases can be extended to account for the effects of various solvents and complexing agents on the rates of diborane hydroborations.

Conclusion

For more than two decades, the role of ether in catalyzing the hydroboration reaction has not been satisfactorily explained. The present kinetic studies and theoretical discussions provide a reasonable explanation for the effects of ether solvents, as well as other Lewis bases, on the rates of the hydroboration reaction. We propose that ethers and other Lewis bases are not directly involved in the actual hydroboration step.[23] They only provide alternative reaction pathways to free boranes with lower activation energies.

Indeed, the catalytic effect of ethers and other Lewis bases on hydroboration is probably a special example of a far more general phenomenon. Replacing a high activation energy step with two parallel lower activation energy steps can dramatically increase the reaction rate. This feature may be applicable to many other systems. Many organometallic compounds exist in dimeric or more highly polymeric forms involving two or more bridge bonds.[24,25] Formation of weak complexes capable of rapid dissociation into the free monomer may provide a means of strongly catalyzing the reactions of such organometallics.

Experimental Section

General procedures for the manipulation of boron reagents have been outlined in Chapter 9 of ref 4c. All glassware, syringes, and needles were oven-dried at 140 °C for several hours. 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. The quantitative analyses of alkenes were carried out on a Varian Model 1200 GLC, equipped with a 0.25-in. injection port with an appropriate liner. Peak integrations were carried out by a disk mechanical integrator or by a Hewlett-Packard digital 3380S integrator. A Miran-1A variable-filter infrared spectrometer from Wilks Scientific Corp. was used to monitor the boron–hydrogen bridge bonds of $(9\text{-BBN})_2$ at 1570 cm^{-1} or the boron–hydrogen terminal bonds of 9-BBN·Lewis base complexes at 2300 cm^{-1}. The ^{11}B NMR spectra were obtained on a Varian XL-100 spectrometer or a Varian FT-80A spectrometer.

Materials. The preparation of $(9\text{-BBN})_2$ and the purification of solvents were described elsewhere.[4c] Dimethyl sulfide was distilled from $(9\text{-BBN})_2$ prior to use. 2,5-Dimethyltetrahydrofuran was distilled over $(9\text{-BBN})_2$ and then stored under nitrogen. The alkanes (Phillips pure grade) employed as internal standard were used as received. The alkenes were distilled under nitrogen from $LiAlH_4$ and then stored under nitrogen. The methanol (Mallinckrodt Spectroquality) and ethanol (anhydrous reagent grade) employed as the quenching reagents were used as received. The amines were distilled under nitrogen from CaH_2 and then stored under nitrogen. Hexanal and cyclohexanone were also distilled under nitrogen prior to use.

Hydroboration of Alkenes with $(9\text{-BBN})_2$ in Various Solvents. The kinetics of the hydroboration of alkenes with $(9\text{-BBN})_2$ in CCl_4, cyclohexane, benzene, diethyl ether, and THF have been described previously.[1] The hydroboration of alkenes (0.200 M) with $(9\text{-BBN})_2$ (0.100 M) in 2,5-dimethyltetrahydrofuran and in the mixed solvent of THF and CCl_4 were similarly monitored with an IR spectrometer at 1570 cm^{-1}. The reaction of 2-methyl-1-pentene (0.400 M), hexanal (0.400 M), and cyclohexanone (0.400 M) with $(9\text{-BBN})_2$ (0.200 M) in Me_2S were also followed by the quenching GLC method as well as by an IR spectrometer monitored at 1570 cm^{-1}. The standard deviation of the rate constants is normally less than 1% of the rate constants when the kinetic data were best fitted with a straight line by using the method of least squares. The complex formation of $(9\text{-BBN})_2$ with pyrrolidine in cyclohexane, benzene, and THF was followed by an IR spectrometer at 1570 cm^{-1} as described previously.[11a]

9-BBN·THF Complex. The amount of the 9-BBN·THF complex in the THF solvent was determined by adding 5.0 mmol of 2-methyl-1-pentene (0.62 mL, 0.42 g) to a rapidly stirred solution of 25 mL of 0.100 M $(9\text{-BBN})_2$ (2.5 mmol) in THF at 25 °C that contained 0.21 g of *n*-octane as an internal standard for GLC analysis. An aliquot (0.5 mL) of the solution was withdrawn and quenched with 0.5 mL of methanol immediately following the addition of 2-methyl-1-pentene. GLC analysis, using the conditions described previously,[1b] exhibited an immediate disappearance of 16% of 2-methyl-1-pentene. This is attributed to the presence of 16% of 9-BBN·THF complex in the solution. The reaction then exhibited simple first-order kinetics. A similar reaction was carried out for the reaction of 2-methyl-1-pentene (0.020 M) with 0.010 M $(9\text{-BBN})_2$ in THF. An initial rapid disappearance of 40% of 2-methyl-1-pentene was observed.

In addition to the quenching GLC method, the hydroboration of 2-methyl-1-pentene with the 9-BBN·THF complex was also followed by a quantitative infrared spectrometer. Unlike previous cases,[1c] the reaction was monitored at 2300 cm^{-1}, corresponding to the absorption peak of the boron–hydrogen terminal bond of the 9-BBN·THF complex. To a solution of 25 mL of $(9\text{-BBN})_2$ (0.100 F, 2.5 mmol) in THF, maintained at 25.0 ± 0.05 °C and pumped 4 mL per minute through a 0.19-mm NaCl IR cell, was added 0.42 g of 2-methyl-1-pentene (0.62 mL, 5.0 mmol). The absorption peak at 2300 cm^{-1} disappeared immediately. When only 0.21 g of 2-methyl-1-pentene (0.31 mL, 2.5 mmol) was added, it also disappeared immediately. However, the peak reappeared after 5 min and reached its maximum absorbance (61% of the starting absorbance) within 15 min. This absorption also disappeared immediately following introduction of an additional 0.105 g of 2-methyl-1-pentene (0.155 mL, 1.25 mmol). Again it reappeared after 5 min and reached its maximum absorbance (37% of the starting absorbance) within 15 min.

9-BBN·SMe_2 Complex. The reactions of alkenes with 9-BBN·SMe_2 in Me_2S were studied by using the same methods employed to study those of the 9-BBN·THF complex. Both the quenching GLC method and the IR method were used to follow the reaction.

Hydroboration of 2-Methyl-1-pentene with 9-BBN·Amine Complex. The 9-BBN·amine complex was prepared by adding 10.0 mmol of amine via a syringe into 18.5 mL of 0.27 M $(9\text{-BBN})_2$ (5.0 mmol) in THF. A 0.21-g sample of *n*-octane was added as an internal standard for GLC analysis. The reaction mixture was then diluted with THF to the desired concentration and stirred at 25.00 ± 0.05 °C for 2 h to ensure complete complex formation. The hydroboration reaction was then started by adding 10.0 mmol of 2-methyl-1-pentene to the reaction mixture. The concentration of 2-methyl-1-pentene became 0.30 M, and the concentration of 9-BBN·amine complex also became 0.30 M. The reaction was followed by the quenching GLC method. The data are shown in Figure 2.

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The effect of excess amine on the reaction rate was also studied. Sufficient trimethylamine was added to form 9-BBN·NMe_3 and provide 50% excess NMe_3. The results are shown graphically in Figure 1. The percentage of complex formation of $(9\text{-BBN})_2$ with various amines was determined by the IR method described previously.[11a]

Competitive Studies of Alkene Pairs. The relative reactivities of alkenes toward $(9\text{-BBN})_2$ in both CCl_4 and THF were studied by using the competitive method. The reaction procedure has been described previously.[1b] Several alkene pairs were chosen for comparison. A summary of the results is given in Table III.

Registry No. $(9\text{-BBN})_2$, 21205-91-4; 9-BBN·THF, 76422-63-4; 9-BBN·SMe_2, 64045-91-6; 9-BBN·NMe_3, 64070-34-4; 9-BBN·*N*-methylpiperidine, 83605-84-9; 9-BBN·(2-Mepy), 70338-10-2; 9-BBN·TMEDA, 64045-93-8; 2-(9-BBN)·TMEDA, 83605-85-0; SMe_2, 75-18-3; CCl_4, 56-23-5; THF, 109-99-9; 2,5-dimethyl-THF, 1003-38-9; 1-hexene, 592-41-6; 2-methyl-1-pentene, 763-29-1; 3,3-dimethyl-1-butene, 558-37-2; cyclopentene, 142-29-0; 2-methyl-2-butene, 513-35-9; 1-methylcyclopentene, 693-89-0; *cis*-3-hexene, 7642-09-3; *cis*-4,4-dimethyl-2-pentene, 762-63-0; hexanal, 66-25-1; cyclohexanone, 108-94-1; cyclohexane, 110-82-7; benzene, 71-43-2; diethyl ether, 60-29-7.

Photochemical and Photophysical Studies of Amines with Excited Flavins. Relevance to the Mechanism of Action of the Flavin-Dependent Monoamine Oxidase‡

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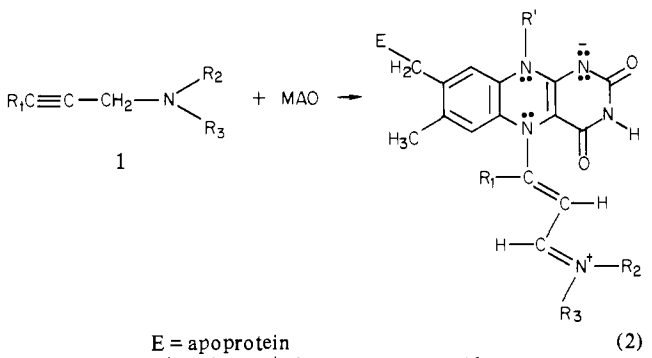
Abstract: The photochemical reactions between 3-methyllumiflavin (3-MLF) and β,γ-acetylenic, β,γ,δ-allenic, and saturated amines, in aqueous and nonhydroxylic solvents, have been investigated. The fluorescence of 3-MLF in nonhydroxylic solvents is efficiently quenched by all amines studied, with values of k_s (the rate constant for quenching of singlet 3-MLF) near the calculated rate of diffusion. Quenching rates in aqueous solution are pH and concentration dependent and indicate that the free amine is required for the observation of fluorescence quenching. Whereas amine quenching of singlet 3-MLF is nonproductive, quenching of triplet 3-MLF leads to adducts that can be isolated from the reaction of the allenic and β,γ-acetylenic amines but that are unstable in the case of saturated amines. The isolated products from β,γ,δ-allenic amines **2a** and **2b** are flavocyanines. The reactions of β,γ-acetylenic amines with triplet 3-MLF give more complicated product mixtures that include flavocyanines and C_{4a},N_5 adducts in similar amounts. These studies are consistent with a pathway involving one-electron transfer from amine to triplet 3-MLF, followed by successive proton and one-electron transfers leading to reduced flavin and iminium ion intermediates.

Introduction

Reactions between flavins and amines are of contemporary interest and can be induced photochemically[2a,d] or by the action of the flavoenzyme mitochondrial monoamine oxidase[2b,c] (E.C. 1.4.3.4, MAO) according to eq 1. A number of β,γ-unsaturated

$$\text{E-Fl} + R_1CH_2NR_2R_3 \rightarrow \text{E-FlH}^- + R_1CH{=}N^+R_2R_3 \xrightarrow{H_2O} R_1CHO + R_2NHR_3 \quad (1)$$

amines[3-5] not only serve as substrates but are also "suicide inhibitors"[6-8] of this enzyme, in that they become covalently linked to the flavin prosthetic group during the course of catalysis. In fact, treatment of MAO with β,γ-acetylenic amines (**1**) leads irreversibly to intensely absorbing adducts that have been characterized as flavocyanines[5,9,10] (eq 2). (Flavocyanines have also been prepared photochemically from the model flavin, 3-methyllumiflavin (3-MLF), and tertiary β,γ-acetylenic amines, but in this case C_{4a},N_5 adducts are formed in substantial amounts (eq 3).[4]) By comparison, β,γ,δ-allenic amines that are strict analogues of acetylenic suicide inhibitors do not yield flavocyanines when they are incubated with MAO but give a product possessing the spectrum of a "reduced (alkylated) flavin".[5,11]



E = apoprotein (2)
R' = ribityl-5'-phosphate AMP residue

To gain a deeper understanding of suicide inhibition of flavoenzymes, it is of interest to model events leading to covalent and irreversible attachment of such latent inhibitors to the target flavin prosthetic group. Although the means of activating the components in the dark, enzymatic process, and in the light-induced

‡Dedicated to Professor William von Eggers Doering on the occasion of his 65th birthday.

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0002-7863/82/1504-7155$01.25/0