centration of $(9\text{-BBN})_2$ at time t, a is the initial absorbance, c is the absorbance at time t, and b is the background absorbance.

The calculations of the rate constants were carried out on a Hewlett-Packard 9820 calculator. The concentrations were substituted into the integrated rate expressions appropriate for each kinetic order. The best straight line was fitted to each set of points by using the method of least squares. The rate constants for the different kinetic orders were obtained numerically as the slopes of the lines.

Registry No. 9-Borabicyclo[3.3.1]nonane dimer, 70658-61-6; cyclopentene, 142-29-0; cyclohexene, 110-83-8; *cis*-3-hexene, 7642-09-3; 1-hexene, 592-41-6; 2-methyl-1-pentene, 763-29-1; 3,3-dimethyl-1-butene, 558-37-2.

Relative Rates and Regioselectivity in the Hydroboration of Substituted Styrenes with 9-Borabicyclo[3.3.1]nonane in Tetrahydrofuran

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Received June 11, 1980

The relative rates of reaction of p-CH$_3$O, p-CH$_3$, unsubstituted, p-F, p-Cl, m-Cl, and m-NO$_2$ styrenes with 9-borabicyclo[3.3.1]nonane (9-BBN) in THF solution at 25 °C have been determined to be 2.95, 1.51, 1.00, 0.89, 0.69, 0.63, and 0.60. The relative rates were established by allowing a mixture of styrene and the substituted styrene to react with a limited amount of 9-BBN (GLC analysis). A Hammett plot, using σ^+, is reasonably linear with $\rho = -0.49$, corresponding to a small buildup of positive charge at the α-carbon of the styrene and reaction with the $B^{\delta+}$–$H^{\delta-}$ bond. 9-BBN gives high regioselectivity in its reactions with the six styrenes tested, the β-phenylethyl alcohol being formed to the extent of 97.4% or higher in all cases. The large steric requirements of the 9-BBN result in the orientation of the B–H bond with B away from the aromatic ring. Several 9-BBN adducts of substituted styrenes have been prepared in pure form.

9-Borabicyclo[3.3.1]nonane (9-BBN)[1,2] has been shown by Brown and co-workers[2-4] to be an exceptionally versatile hydroborating reagent, easy to handle as the dimeric solid (even in air) and in solution (nitrogen atmosphere required), and of great thermal stability. For reactive alkenes, hydroboration rates have recently been shown[5] to be first order in 9-BBN dimer and independent of alkene concentration (rate-determining dissociation of the dimer), while for less reactive olefins, the rates are half order in 9-BBN dimer and first order in alkene (rate-determining reaction of the 9-BBN monomer with the alkene). Thus, in order to assess the relative reactivities of alkenes, it is necessary to use competitive experiments where mixtures of alkenes react with a limited amount of 9-BBN.[6] From these previous experiments[6] it is clear that the rates of reaction of 9-BBN are subject to large steric effects but that 9-BBN is nevertheless quite sensitive to electronic influences, presumably due to the strained bridging >BH moiety. For instance, using the competitive technique, Brown, Liotta, and Scouten[6] showed that p-methoxystyrene, unsubstituted styrene, and p-(trifluoromethyl)styrene had relative reactivities of 14.0:1:0.2 toward 9-BBN, whereas Klein, Dunkelblum, and Wolff[7] found that the overall rate of reaction of styrenes with diborane changes very little with substituents ranging from methoxy to chloro. As a first step in a projected isotope effect study of the mechanisms of hydroboration of substituted styrenes, we have extended the competitive rate experiments of 9-BBN to include reactions with several additional substituted styrenes.

One of the most useful features of 9-BBN is its extremely high regioselectivity in hydroboration reactions.[3,8,9] For instance, in the diborane hydroboration–alkaline hydrogen peroxide oxidation of styrene, 2-phenylethanol and 1-phenylethanol were formed[10,11] in 81% and 19% relative yields, while with 9-BBN the relative yields were 98.5% and 1.5%.[3,8,9] For optimum usefulness and ease of interpretation, our projected isotope effect study required a reaction proceeding to only one product, and it was hoped that 9-BBN reactions with substituted styrenes would also be highly regioselective. Since the regioselectivity of the reactions of 9-BBN with substituted styrenes did not seem to have been reported, we have carried out such a study.

Scheme I

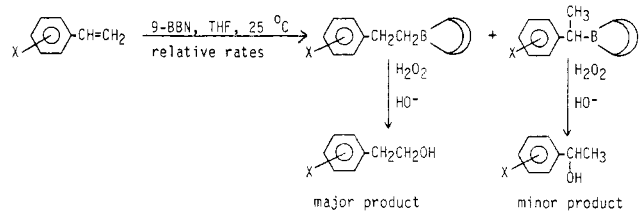

Table I. Relative Reactivities of Substituted Styrenes toward 9-BBN in THF at 25 ± 0.1 °C

substituent	k_X/k_H ± std dev	substituent	k_X/k_H ± std dev
p-CH$_3$O	2.95 ± 0.22	p-Cl	0.69 ± 0.01
p-CH$_3$	1.51 ± 0.04	m-Cl	0.63 ± 0.02
none	1.00	m-NO$_2$	0.60 ± 0.04
p-F	0.89 ± 0.03		

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(1) Koster, R. *Angew. Chem.* **1960**, *72*, 626–627.

(2) Knights, E. F.; Brown, H. C. *J. Am. Chem. Soc.* **1968**, *90*, 5280–5281.

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(4) Brown, H. C.; Krishnamurthy, S.; Yoon, M. N. *J. Org. Chem.* **1976**, *41*, 1778–1791.

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

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(8) Knights, E. F.; Brown, H. C. *J. Am. Chem. Soc.* **1968**, *90*, 5281–5283.

(9) Scouten, C. G.; Brown, H. C. *J. Org. Chem.* **1973**, *38*, 4092–4094.

(10) Brown, H. C.; Sharp, R. L. *J. Am. Chem. Soc.* **1966**, *88*, 5851–5854.

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The 9-BBN adducts of several substituted styrenes have been isolated in pure form (see Scheme I).

Results and Discussion

In the competitive rate experiments,[4,6] an equimolar mixture of styrene and the substituted styrene in THF was allowed to react at 25 ± 0.1 °C with the amount of 9-BBN equivalent to that of one of the styrenes. The amounts of residual styrenes after various times were followed by GLC using an internal saturated hydrocarbon standard and a short THEED stripper column before the main analytical column to retain the intermediate organoboranes. In all cases the initial 1:1 styrene–substituted styrene ratio changed rapidly and within a short time leveled off at a constant value which was maintained for many hours. Eventually (after 5–20 h) the amount of residual styrenes began to decrease, probably due to polymerization. Five to ten samples, starting with the 1-h sample, were analyzed at various times during this 5–20-h plateau period, and for each sample the relative rate, k_X/k_H, was calculated by using the Ingold–Shaw expression:[12] $k_X/k_H = (\log SX_0 - \log SX)/(\log SH_0 - \log SH)$, where SX_0 and SH_0 are the initial concentrations and SX and SH are the residual concentrations of the substituted and unsubstituted styrenes. The results are shown in Table I. The material balances are uniformly good[13] in these experiments, and duplicate experiments gave agreement within the reported error limits. In particular, three experiments using three different GLC columns all gave the same result for p-methoxystyrene, $k_{CH_3O}/k_H = 2.95$, in contrast to the value of 14.0 reported by Brown, Liotta, and Scouten.[6] We know of no reason for this discrepancy.[14]

Although the variations in rate with substituent are not very large, they are substantially greater than those observed by Klein, Dunkelblum, and Wolff[7] in the corresponding reductions with diborane, demonstrating the stronger response of 9-BBN than of diborane to electronic differences in alkenes. A Hammett plot of the data in Table I using σ values is badly scattered, but a reasonably good linear plot is obtained by using σ^+, with $\rho = -0.49$ (correlation coefficient 0.94). This is consistent with the buildup of a small positive charge on the styrene carbon α to the ring, in accordance with expectation from the polarization of the $B^{\delta+}-H^{\delta-}$ bond and high regioselectivity to give nearly exclusive β-phenylethyl derivatives.

These electronic influences on the rates of the reaction of 9-BBN with substituted styrenes are not reflected in large differences in regioselectivity, as shown by our hydroboration–oxidation experiments. With diborane, Brown and Sharp[10] showed that hydroboration–oxidation of substituted styrenes gave varying amounts of α and β products (mainly the phenylethyl alcohols), with log (β/α) giving a linear plot with σ^+. Electron-donating substituents resulted in high yields of the β products, while electron-withdrawing groups led to up to 37% α products. The results of our similar hydroboration–oxidation experiments using 9-BBN are given in Table II.

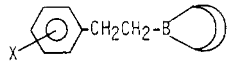
All of the compounds showed the high regioselectivity characteristic[3,8,9] of 9-BBN. There is no trend with the electronic nature of the substituent. The contrast between the high regioselectivity of 9-BBN compared to that of diborane observed by Brown's group for styrene[3,8,9] carries over to substituted styrenes as well. Evidently the electronic influences are important in determining the rate of hydroboration, but only after the primary orientation of the B–H bond relative to the styrene double bond is established by steric factors.

Table II. Directive Effects in the Hydroboration–Oxidation of Substituted Styrenes Using 9-BBN

substituent	alcohol yield,[a] %	% alcohol product	
		α-ol	β-ol
p-CH_3O	94	1.1	98.9
p-CH_3	84	2.6	97.4
none	82	2.0	98.0
p-F	98	2.0	98.0
p-Cl	99	0.7	99.3
p-NO_2	88	2.4	97.6

[a] GLC yield, based on styrene used.

Table III. 9-(2-Arylethyl)-9-borabicyclo[3.3.1]nonanes



X	% yield (distilled)	bp, °C (mmHg)	^1H NMR data, δ ($CDCl_3$)
p-CH_3O	70	126–127 (0.24)	6.65 (m, 4 H, Ar), 3.64 (s, 3 H, CH_3O), 2.65 (t, 2 H, $J = 4$ Hz, $ArCH_2$), 2.30–0.65 (16 H, 9-BBN–CH_2)
p-CH_3	71	117–118 (0.18)	6.78 (~s, 4 H, Ar), 2.85–2.28 (m, 2 H, $ArCH_2$), 2.20 (s, 3 H, CH_3), 2.00–0.75 (16 H, 9-BBN–CH_2)
H	76	119–120 (0.35)	7.00 (s, 5 H, Ph), 2.78 (t, 2 H, $J = 3.5$ Hz, $PhCH_2$), 2.30–0.90 (16 H, 9-BBN–CH_2)
p-F	64	109–110 (0.34)	6.90–6.35 (m, 4 H, Ar), 2.70 (t, 2 H, $J = 3$ Hz, $ArCH_2$), 2.35 (t, 2 H, $J = 3$ Hz, CH_2B), 1.90–0.70 (14 H, 9-BBN)
p-Cl	73	162–163 (7.0), 124–125 (0.25)	6.90 (m, 4 H, Ar), 2.70 (t, 2 H, $J = 4$ Hz, $ArCH_2$), 2.15–0.65 (16 H, 9-BBN–CH_2)
m-Cl	71	122–123 (0.28)	6.68 (m, 4 H, Ar), 2.68 (t, 2 H, $J = 3$ Hz, $ArCH_2$), 2.00–0.65 (16 H, 9-BBN–CH_2)

Brown and Sharp[10] observed the formation of significant amounts of hydrolysis product, p-nitroethylbenzene, during the oxidation of the diborane hydroboration product of p-nitrostyrene. We made a careful GLC search for p-nitroethylbenzene in the products from the oxidation of the 9-BBN adduct of p-nitrostyrene and found none. (No ethylbenzenes were formed from the other styrenes either.) Here again, 9-BBN is superior to diborane as a "clean" hydroborating agent.

For the most part, 9-BBN adducts with alkenes are used in situ, but as a part of this research we have isolated several of them (see Experimental Section and Table III) in pure form. When the solvent was removed in preparation for distillation, the m-nitrostyrene–9-BBN adduct

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(12) Ingold, C. K.; Shaw, F. R. J. Chem. Soc. 1927, 2918–2926.

(13) When p-nitrostyrene was used, a plateau of sorts was reached well before half of the total styrenes had reacted, indicating that some side reaction was using 9-BBN. This same behavior was observed by Brown and Sharp[10] in their similar reaction of p-nitrostyrene with diborane. For this reason, p-nitrostyrene is not included in Table I.

(14) While it is not clear from their report, it may be that Brown, Liotta, and Scouten[6] did not carry out a direct competition between styrene and p-methoxystyrene.

decomposed with almost explosive force.

Experimental Section

Materials and General Methods. Tetrahydrofuran was purified by distillation over sodium in the presence of benzophenone under dry nitrogen gas. The styrenes used were commercial materials of highest purity and were further purified by distillation over lithium aluminum hydride when necessary. The internal standards, reference samples, and 9-BBN solid and 0.5 M solution in THF were obtained commercially. All operations were carried out under dry nitrogen and followed standard procedures.[15] All glassware and syringe needles were oven dried at 130 °C, assembled while hot, and cooled under a stream of dry nitrogen gas.

All GLC analyses were carried out on a Varian Aerograph Series 2800 instrument equipped with a flame-ionization detector attached in series with a LDC 302 computing integrator and a Sargent Recorder Model SR of 1.25-mV range. The NMR spectra were taken on a Varian Anaspect EM-360 60-MHz NMR spectrometer using tetramethylsilane as an internal reference.

Competitive Relative Rate Experiments. The procedure generally followed that of Brown, Liotta, and Scouten.[6] A THF solution of 0.0025 mol (3 mL) each of styrene and the substituted styrene together with a weighed quantity of a hydrocarbon internal standard was allowed to react in a magnetically stirred system with 0.0025 mol (5 mL) of a standard 0.5 M solution of 9-BBN in THF under a dry nitrogen atmosphere at 25 ± 0.1 °C. All material transfers were carried out by syringes which had been flushed with dry nitrogen. Periodically, minute samples were withdrawn by syringe and analyzed for residual styrenes by GLC, with the internal standard used to determine response factors and yields. Short (a few inches of $^{1}/_{4}$-in. diameter aluminum) THEED stripper columns (to remove organoborane compounds) were used in series with SE-30 or Carbowax 20M on Chromosorb W-HP (100/120 mesh) $^{1}/_{8}$-in. aluminum columns. The hydrocarbon standards used were undecane, dodecane, and hexdecane, the choice depending on the retention times of the styrenes. Within 1 h or less the residual styrenes ratio reached a constant value, which remained unchanged for periods of 5–20 h, after which time the amounts of residual styrenes gradually decreased. The relative rates were calculated[12] from the samples taken in the plateau region and are given in Table I.

Regioselectivity Experiments. The various styrenes were hydroborated and oxidized with alkaline hydrogen peroxide in the standard way.[9,15] The yields of the isomeric 1- and 2-phenylethanols were determined by GLC analysis with dodecane or one of the other substituted phenylethyl alcohols as internal standards. The reliability of the analysis for the minor component was checked by analysis of known mixtures of authentic samples in the presence of the internal standard used. The results are shown in Table II.

Preparation of 9-(2-Arylethyl)-9-borabicyclo[3.3.1]nonanes. A THF solution of 0.02 mol (40 mL of a 0.5 M solution) of 9-BBN was added slowly with stirring to 0.02 mol of the appropriate styrene in 10 mL of THF under a dry nitrogen atmosphere. After 16 h the solvent was removed on a rotary evaporator. The crude yields of the light pale yellow oils were all quantitative. **Caution**: Although stable in THF solution, the *m*-nitrostyrene–9-BBN adduct decomposed violently when the solvent was removed. (After this experience, no attempt was made to prepare the *p*-nitrostyrene adduct.) The crude adducts were transferred by disposable plastic syringes to the vacuum distillation apparatus, which contained a dry nitrogen atmosphere. The crude material was stirred magnetically during the vacuum distillation, and the colorless distilled samples were sealed under dry nitorgen. The adducts generated thick white fumes when exposed to air but did not catch fire. The details of the preparations are given in Table III.

Acknowledgment. This work was supported by National Science Foundation Grant CHE-78-09809. We are grateful to Professor W. L. Meyer for a helpful discussion.

Registry No. *p*-Methoxystyrene, 637-69-4; *p*-methylstyrene, 622-97-9; styrene, 100-42-5; *p*-fluorostyrene, 405-99-2; *p*-chlorostyrene, 1073-67-2; *m*-chlorostyrene, 2039-85-2; *m*-nitrostyrene, 586-39-0; *p*-nitrostyrene, 100-13-0; 9-(2-(4-methoxyphenyl)ethyl)-9-borabicyclo[3.3.1]nonane, 75400-50-9; 9-(2-(4-methylphenyl)ethyl)-9-borabicyclo[3.3.1]nonane, 75400-51-0; 9-(2-phenylethyl)-9-borabicyclo[3.3.1]nonane, 67753-90-6; 9-(2-(4-fluorophenyl)ethyl)-9-borabicyclo[3.3.1]nonane, 75400-52-1; 9-(2-(4-chlorophenyl)ethyl)-9-borabicyclo[3.3.1]nonane, 75400-53-2; 9-(2-(3-chlorophenyl)ethyl)-9-borabicyclo[3.3.1]nonane, 75400-54-3; 4-methoxy-α-methylbenzenemethanol, 3319-15-1; α,4-dimethylbenzenemethanol, 536-50-5; α-methylbenzenemethanol, 98-85-1; 4-fluoro-α-methylbenzenemethanol, 403-41-8; 4-chloro-α-methylbenzenemethanol, 3391-10-4; α-methyl-4-nitrobenzenemethanol, 6531-13-1; 4-methoxybenzeneethanol, 702-23-8; 4-methylbenzeneethanol, 699-02-5; benzeneethanol, 60-12-8; 4-fluorobenzeneethanol, 7589-27-7; 4-chlorobenzeneethanol, 1875-88-3; 4-nitrobenzeneethanol, 100-27-6; 9-BBN, 280-64-8.

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(15) We have found particularly helpful the many detailed experimental procedures and the chapter "Laboratory Operations with Air Sensitive Substances" by Kramer, Levy, and Midland in: Brown, H. C. "Organic Syntheses Via Boranes"; Wiley: New York, 1975.

1,3-Diazepinones. 2. The Correct Structure of Squamolone as 1-Carbamoyl-2-pyrrolidinone and Synthesis of Authentic Perhydro-1,3-diazepine-2,4-dione

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Received September 3, 1980

The natural product squamolone, previously reported as 4-oxoperhydro-1,3-diazepin-2-one (1), was found to be instead 1-carbamoyl-2-pyrrolidinone (2). An unequivocal synthesis of the diazepinedione 1 starting from glutaric acid monoamide (6) produced the desired compound in five steps. Diborane reduction of 1 yielded the known perhydro-1,3-diazepin-2-one (10, tetramethyleneurea), confirming the seven-membered-ring structure of 1. A detailed analysis of the IR, NMR, and mass spectra of squamolone (2) and its isomer 1 is presented. A one-step synthesis of squamolone (2) starting with 4-aminobutyric acid 3 is reported.

The functionalized perhydro-1,3-diazepin-2-one system has been the subject of recent interest in view of the very potent inhibition of cytidine deaminase exhibited by some of its nucleosides.[1] The 5-oxo- and 5-hydroxyperhydro-