Selective Reductions. XVI. Reaction of Disiamylborane in Tetrahydrofuran with Selected Organic Compounds Containing Representative Functional Groups

Herbert C. Brown, D. B. Bigley,[1] S. K. Arora,[2] and Nung Min Yoon[2]

Contribution from the Richard B. Wetherill Laboratory of Purdue University, Lafayette, Indiana 47907. *Received May 29, 1970*

Abstract: The approximate rates and the stoichiometry of the reaction of excess disiamylborane with 56 selected organic compounds containing representative functional groups under standard conditions (tetrahydrofuran solution, 0°) were determined in order to establish the utility of the reagent as a selective reducing agent and to compare its characteristics with those of diborane and the aluminohydrides previously studied. The rates of hydrogen evolutions from 1-hexanol, benzyl alcohol, 3-hexanol, and phenol are fast, whereas 3-ethyl-3-pentanol, *n*-hexylamine, and thiols failed to evolve hydrogen under the standard conditions. Aldehydes and ketones reduce rapidly; however, benzophenone is reduced at only a moderate rate. Cinnamaldehyde is reduced to the cinnamyl alcohol stage rapidly, followed by a slow hydroboration of the double bond. The rates of reduction of quinones are slow. Acids evolve only hydrogen without reduction. Acetic anhydride is reduced rapidly, but only to the half-reduction stage. Cyclic anhydrides and acyl chlorides are not reduced. Esters are inert. However, γ-butyrolactone is rapidly reduced to γ-hydroxybutyraldehyde. Isopropenyl acetate undergoes rapid hydroboration, elimination, and rehydroboration. 1,2-Butylene oxide and cyclohexene oxide are almost inert to this reagent, whereas styrene oxide and 1-methyl-1,2-cyclohexene oxide react, but not in a simple manner. Primary amides evolve only hydrogen without undergoing reduction, whereas tertiary amides are cleanly reduced to the corresponding aldehydes. Nitriles are reduced very slowly. 1-Nitropropane is inert, whereas nitrobenzene is reduced slowly. Azoxybenzene is slowly reduced to the azobenzene stage. Cyclohexanone oxime liberates hydrogen with no indication of reduction. Phenyl isocyanate undergoes reduction to the imine stage at a moderate rate. Pyridine *N*-oxide is slowly reduced to pyridine. Finally, dimethyl sulfoxide is reduced at a moderate rate, whereas the other sulfur compounds tested, disulfides, sulfide, sulfone, tosylate, and sulfonic acids, are inert to this reagent under the standard conditions.

Disiamylborane has been shown to be an excellent selective hydroborating reagent.[3] The reducing properties of this reagent have not yet been subjected to the same kind of detailed study although preliminary experiments[4] have indicated that disiamylborane is highly promising for such applications. Therefore, we decided to undertake a detailed study of the full scope of the reducing characteristics of this reagent.

We recently carried through systematic studies of the approximate rates and the stoichiometry of the reaction of diborane[5] and aluminohydrides[6] in tetrahydrofuran solution at 0° with a standard list of compounds representative of the more common functional groups. In order to obtain information defining the characteristics of disiamylborane for comparison with those of diborane and the aluminohydrides already examined, we decided to undertake a systematic study of the reaction of disiamylborane with the standard list under the standard conditions.

Results and Discussion

Procedure for Rate and Stoichiometry Studies. The procedure adopted was to add 5 mmol of the organic compound to 20 mmol of disiamylborane in sufficient tetrahydrofuran to give 20 ml of solution at 0°. Thus the ratio of hydride to compound was 4:1, and the solution was 1.00 *M* in hydride and 0.25 *M* in compound. The solution was maintained at 0°, and aliquots were removed at appropriate intervals and analyzed for residual "hydride." In this manner, it was possible both to establish the rate at which the reduction proceeds and the stoichiometry of the reaction, *i.e.*, the number of hydrides utilized per mole of compound. The reaction was halted when two or more successive analyses indicated no change in the "hydride" utilized. All experiments were carried out under nitrogen.

Alcohols, Phenols, Amines, and Thiols. The primary alcohols, the secondary alcohol, and phenol liberated hydrogen instantly and quantitatively. However, the tertiary alcohol, 3-ethyl-3-pentanol, *n*-hexylamine, and the thiols did not react with this reagent. This suggests the possibility of protecting primary or secondary hydroxyl groups in a molecule by converting them selectively to the corresponding disiamylborinates, permitting the reaction of residual tertiary hydroxyl or amino functional groups in the same molecule with

---

[1] American Cyanamide Postdoctoral Research Associate.

[2] Postdoctoral Research Associates on Research Grants DA 31-124 ARO(D)-117 and -453 supported by the U. S. Army Research Office (Durham).

[3] (a) H. C. Brown and G. Zweifel, *J. Amer. Chem. Soc.*, **83**, 1241 (1961); (b) H. C. Brown and A. W. Moerikofer, *ibid.*, **83**, 3417 (1961); (c) G. Zweifel, K. Nagase, and H. C. Brown, *ibid.*, **84**, 190 (1962); (d) G. Zweifel, N. Ayyangar, and H. C. Brown, *ibid.*, **85**, 2072 (1963); (e) H. C. Brown and A. W. Moerikofer, *ibid.*, **85**, 2063 (1963); (f) H. C. Brown and K. A. Keblys, *ibid.*, **86**, 1791 (1964).

[4] These were reported in our previous communications; see (a) H. C. Brown and D. B. Bigley, *ibid.*, **83**, 486 (1961); (b) *ibid.*, **83**, 3166 (1961); (c) H. C. Brown and V. Varma, *ibid.*, **88**, 2871 (1966). We reported that in contrast to diborane, disiamylborane does not reduce carboxylic acids, although γ-lactones are reduced to the corresponding aldehydes in good yields, and in the reduction of monocyclic ketones, this reagent reveals unusual stereospecific capabilities in comparison with diborane and the aluminohydrides.

[5] H. C. Brown, P. Heim, and N. M. Yoon, *J. Amer. Chem. Soc.*, **92**, 1637 (1970).

[6] (a) H. C. Brown, P. M. Weissman, and N. M. Yoon, *ibid.*, **88**, 1458 (1966); (b) H. C. Brown and N. M. Yoon, *ibid.*, **88**, 1464 (1966); (c) H. C. Brown and P. M. Weissman, *ibid.*, **87**, 5614 (1965); (d) H. C. Brown and P. M. Weissman, *Israel J. Chem.*, **1**, 430 (1963).

Table I. Reaction of Disiamylborane with Representative "Active Hydrogen" Compounds in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
1-Hexanol	0.5	1.07	1.07	0.00
	1.0	1.07	1.07	0.00
Benzyl alcohol	0.5	0.99	1.03	0.04
	1.0	0.99	1.03	0.04
3-Hexanol	0.5	0.99	1.03	0.04
	1.0	0.99	1.03	0.04
3-Ethyl-3-pentanol	0.5	0.00	0.00	0.00
	1.0	0.00	0.00	0.00
Phenol	0.5	1.05	1.06	0.01
	1.0	1.05	1.06	0.01
n-Hexylamine[c]	0.5	0.00	0.00	0.00
	1.0	0.00	0.00	0.00
1-Hexanethiol	0.5	0.00	0.00	0.00
	1.0	0.00	0.00	0.00
Benzenethiol	0.5	0.00	0.00	0.00
	1.0	0.00	0.00	0.00

[a] 5.0 mmol of compound to 20 mmol of disiamylborane (20 mmol of hydride) in 20 ml of solution; 0.25 *M* in compound and 1.00 *M* in hydride. [b] Mmoles/mmol of compound. [c] Refluxing concentrated hydrochloric acid was used to decompose aliquots.

Table II. Reaction of Disiamylborane with Representative Aldehydes and Ketones in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
Caproaldehyde	0.5	0.00	0.89	0.89
	1.0	0.00	0.96	0.96
	3.0	0.00	0.97	0.97
Benzaldehyde	0.5	0.00	0.94	0.94
	1.0	0.00	0.97	0.97
	3.0	0.00	1.00	1.00
2-Heptanone	0.5	0.00	0.83	0.83
	1.0	0.00	0.98	0.98
	3.0	0.00	1.00	1.00
Norcamphor[c]	0.5	0.04	0.98	0.94
	1.0	0.04	1.01	0.97
	3.0	0.04	1.01	0.97
Acetophenone	0.5	0.00	0.60	0.60
	1.0	0.00	0.72	0.72
	3.0	0.00	0.88	0.88
	6.0	0.00	1.03	1.03
	12.0	0.00	1.03	1.03
Benzophenone	0.5	0.00	0.22	0.22
	1.0	0.00	0.31	0.31
	3.0	0.00	0.41	0.41
	6.0	0.00	0.52	0.52
	12.0	0.00	0.61	0.61
	24.0	0.00	0.98	0.98
Cinnamaldehyde	0.5	0.02	1.11	1.09
	1.0	0.02	1.24	1.22
	3.0	0.02	1.36	1.34
	6.0	0.02	1.54	1.52
	12.0	0.02	1.71	1.69
	24.0	0.02	2.00	1.98

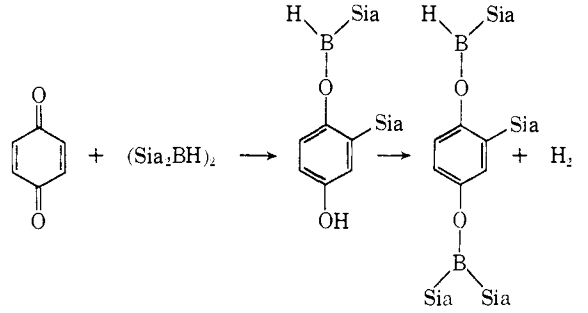
[a] See Table I, footnote *a*. [b] See Table I. footnote *b*. [c] Glpc analysis showed 8% *exo*- and 92% *endo*-norbornanol.

appropriate reagents, such as acylating agents. The results are summarized in Table I.

Aldehydes and Ketones. The aldehydes and ketones examined all consumed one hydride, indicating reduction to the corresponding alcohols. Cinnamaldehyde consumed two hydrides, the first being used rapidly in 30 min and the second much more slowly. The initial fast reaction involves reduction of the aldehyde group, followed by a slow hydroboration of the double bond. This suggests that it should be possible with this bulky reagent to reduce aldehyde groups selectively in the presence of carbon–carbon double bonds. The reduction of benzophenone was considerably slower than that of the other carbonyl compounds, a trend similar to that observed with diborane.

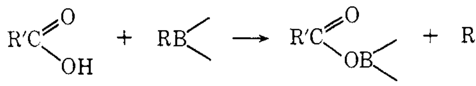
The reduction of norcamphor resulted in 8% *exo*- and 92% *endo*-norbornanol. This was unexpected in view of the high stereospecificity observed with diborane, 2% *exo*- and 98% *endo*-norbornanol. On the other hand, we observed the formation of 79% *cis*-2-methylcyclohexanol in the reduction of 2-methylcyclohexanone with disiamylborane, whereas diborane produces a product containing only 26% of the cis isomer. We are in a position to report the results of a detailed study of the stereochemistry of reduction of ketones by dialkylboranes.[4c] The results are summarized in Table II.

Quinones. *p*-Benzoquinone evolved 0.71 mol of hydrogen rapidly, with the hydride uptake for reduction only 0.27 in 3 hr, a value which did not increase even over 24 hr. A possible mechanism which consumes hydride only for hydrogen evolution involves alkyl migration[7] (eq 1). However, this does not explain the partial hydrogen evolution (0.71). Moreover, when the reaction mixture was oxidized with alkaline hydrogen peroxide, all of the siamyl groups were recovered as the corresponding alcohol. This clearly shows that no alkyl migration occurs, at least during the first ~70% hydrogen evolution. We deferred further investigation of this reaction. The reaction of anthraquinone was very slow, consuming only 0.85 total hydride in 24 hr at room temperature. The results are summarized in Table III.



(1)

Carboxylic Acids and Derivatives. Both caproic acid and benzoic acid liberated hydrogen quantitatively and rapidly. However, no reduction was observed. This is in contrast to the facile reduction of these acids with diborane. Since all of the hydride utilized appeared as hydrogen evolved, we are not observing any hydrocarbon formation[8] (eq 2).



(2)[8]

Acetic anhydride consumed two hydrides rapidly, with only a sluggish reduction thereafter. On the other hand, the two cyclic anhydrides, succinic and

---

(7) A facile alkyl migration in the reaction of trialkylboron and *p*-benzoquinone has been reported: M. F. Hawthorne and M. Reintjes, *J. Amer. Chem. Soc.*, **87**, 4585 (1965).

(8) H. C. Brown and K. Murray, *ibid.*, **81**, 4108 (1959).

Table III. Reaction of Disiamylborane with Representative Quinones in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
p-Benzoquinone	0.5	0.71	0.82	0.11
	1.0	0.71	0.95	0.24
	3.0	0.71	0.98	0.27
	6.0	0.71	0.99	0.28
	12.0	0.71	0.99	0.28
	24.0	0.71	0.98	0.27
Anthraquinone[c]	1.0		0.22	0.22
	3.0	0.02	0.23	0.21
	6.0	0.04	0.25	0.21
	12.0	0.07	0.30	0.23
	24.0	0.11	0.34	0.23
	24.0[d]	0.28	0.85	0.57

[a] See Table I, footnote *a*. [b] See Table I, footnote *b*. [c] Reverse addition (disiamylborane solution in tetrahydrofuran was added to a suspension of anthraquinone in tetrahydrofuran). [d] At 25°.

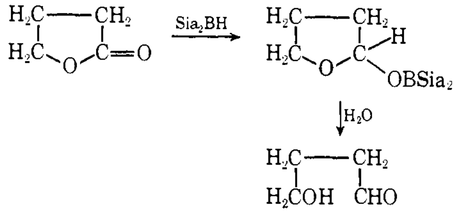
phthalic anhydride, failed to react. Caproyl chloride and benzoyl chloride also proved inert to this reagent. The results are summarized in Table IV.

Table IV. Reaction of Disiamylborane with Representative Carboxylic Acids and Acyl Derivatives in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
Caproic acid	0.5	1.02	1.05	0.03
	1.0	1.02	1.08	0.06
	3.0	1.02	1.08	0.06
Benzoic acid	0.5	1.03	1.03	0.00
	1.0	1.03	1.03	0.00
	3.0	1.03	1.03	0.00
Acetic anhydride	0.5	0.00	1.97	1.97
	1.0	0.00	1.97	1.97
	3.0	0.00	1.97	1.97
	24.0	0.14	2.25	2.11
Succinic anhydride	0.5	0.00	0.01	0.01
	1.0	0.00	0.01	0.01
	3.0	0.00	0.04	0.04
Phthalic anhydride	0.5	0.00	0.01	0.01
	1.0	0.00	0.01	0.01
	3.0	0.00	0.02	0.02
Caproyl chloride	0.5	0.00	0.00	0.00
	1.0	0.00	0.03	0.03
	3.0	0.00	0.00	0.00
Benzoyl chloride	0.5	0.00	0.00	0.00
	1.0	0.00	0.00	0.00
	3.0	0.00	0.03	0.03

[a] See Table I, footnote *a*. [b] See Table I, footnote *b*.

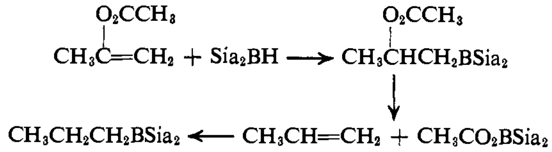
Esters and Lactones. Esters were not reduced by this reagent under the standard conditions. However, a lactone, γ-butyrolactone, reacted rapidly, consuming one hydride in 1 hr corresponding to partial reduction to the hydroxyaldehyde (eq 3). Indeed, we could obtain a 74% yield of γ-hydroxybutyraldehyde from γ-butyrolactone. The reduction of phthalide was very slow at 0°. However, it was possible to obtain a 77% yield of hydrophthalide in 18 hr at room temperature.



(3)

This simple reduction of γ-lactones to the corresponding hydroxyaldehydes appears to be quite general and provides a simple, convenient route to these reactive substances.[9]

Isopropenyl acetate consumed two hydrides at a moderate rate, involving hydroboration of the double bond, β-elimination,[10] and hydroboration of the propylene formed in the elimination stage (eq 4). Oxidation



$$\mathrm{CH_3\overset{O_2CCH_3}{\overset{|}{C}}{=}CH_2 + Sia_2BH \longrightarrow CH_3\overset{O_2CCH_3}{\overset{|}{C}}HCH_2BSia_2 \longrightarrow CH_3CH{=}CH_2 + CH_3CO_2BSia_2;\quad CH_3CH{=}CH_2 \longrightarrow CH_3CH_2CH_2BSia_2} \tag{4}$$

of the reaction product (24 hr, 0°) indicated a 96% yield of 1-propanol. The corresponding reaction with diborane utilizes four hydrides relatively rapidly.[5] The difference in the stoichiometry evidently arises from the ready reduction of the acetoxyboron intermediate by diborane and the inertness of this intermediate toward disiamylborane. (This postulated intermediate is identical with the reaction product of carboxylic acids and disiamylborane discussed earlier.)

The results of these studies of the reaction of representative esters and lactones with disiamylborane are summarized in Table V.

Table V. Reaction of Disiamylborane with Representative Esters and Lactones in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
Ethyl caproate	0.5	0.00	0.00	0.00
	1.0	0.00	0.00	0.00
	3.0	0.00	0.00	0.00
Ethyl benzoate	0.5	0.02	0.02	0.00
	1.0	0.02	0.05	0.03
	3.0	0.02	0.05	0.03
Phenyl acetate	0.5	0.03	0.03	0.00
	1.0	0.03	0.06	0.03
	3.0	0.03	0.05	0.02
γ-Butyrolactone	0.5	0.00	0.76	0.76
	1.0	0.00	1.02	1.02
	3.0	0.00	1.02	1.02
Phthalide	0.5	0.00	0.08	0.08
	1.0	0.00	0.05	0.05
	3.0	0.00	0.05	0.05
	38.0	0.00	0.60	0.60
Isopropenyl acetate	0.5	0.00	1.06	1.06
	1.0	0.00	1.46	1.46
	3.0	0.00	1.89	1.89
	6.0	0.00	2.01	2.01

[a] See Table I, footnote *a*. [b] See Table I, footnote *b*.

---

(9) A number of interesting applications of disiamylborane for this selective reduction of such lactones have been reported: W. R. Vaughan, C. T. Goetschel, M. H. Goodrow, and C. L. Warren, *J. Amer. Chem. Soc.*, **85**, 2282 (1963); F. J. McQuillin and R. B. Yeats, *J. Chem. Soc.*, 4273 (1965); P. Kohn, R. H. Samaritano, and L. M. Lerner, *J. Amer. Chem. Soc.*, **87**, 5475 (1965); G. Buchi, D. M. Foulkes, M. Kurono, and G. F. Mitchell, *ibid.*, **88**, 4534 (1966); R. W. Kierstead and A. Faraone, *J. Org. Chem.*, **32**, 704 (1967); T. A. Giudici and A. L. Fluharty, *ibid.*, **32**, 2043 (1967); P. Kohn, L. M. Lerner, A. Chan, Jr., and S. D. Ginocchio, C. A. Zitrin, *Carbohyd. Res.*, **7**, 21 (1968).

(10) H. C. Brown and O. J. Cope, *J. Amer. Chem. Soc.*, **86**, 1801 (1964).

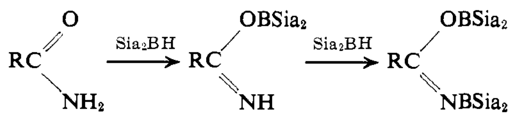
Epoxides. The reactions of 1,2-butylene oxide and cyclohexene oxide with the reagent were very sluggish. However, the reaction of styrene oxide proceeded beyond the stoichiometric point, revealing 2.56 hydride uptake in 72 hr (1.0 hydride uptake is necessary for simple reduction to the corresponding alcohols, 1-, and 2-phenylethanol). The reaction of 1-methyl-1,2-cyclohexene oxide also proceeds slowly, accompanied by hydrogen evolution, indicating approximately one hydride uptake for reduction and one hydride uptake for hydrogen evolution in 48 hr at 0°. These deviations from the behavior expected for simple reduction are very similar to those observed in the reactions of these epoxides with diborane.[5] A detailed study of the reaction of epoxides with hydride reagents has been completed and will be reported separately.[11] The results are summarized in Table VI.

Table VI. Reaction of Disiamylborane with Representative Epoxides in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
1,2-Butylene oxide	0.5	0.00	0.02	0.02
	1.0	0.00	0.08	0.08
	3.0	0.00	0.07	0.07
Styrene oxide	0.5	0.05		
	1.0	0.05	0.15	0.10
	3.0	0.05	0.41	0.36
	6.0	0.05	0.71	0.66
	12.0	0.05	1.25	1.20
	24.0	0.05	1.79	1.74
	48.0	0.05	2.36	2.31
	72.0	0.05	2.61	2.56
Cyclohexene oxide	0.5	0.00	0.02	0.02
	1.0	0.00	0.02	0.02
	3.0	0.00	0.04	0.04
1-Methyl-1,2-cyclohexene oxide	3.0	0.38	0.60	0.22
	6.0	0.53	0.96	0.43
	24.0	0.85	1.85	1.00
	48.0	0.85	1.90	1.11

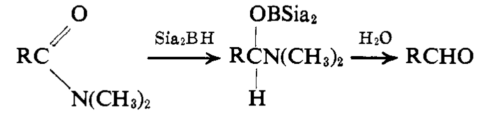
[a] See Table I, footnote *a*. [b] See Table I, footnote *b*.

Amides and Nitriles. Primary amides evolved 2 equiv of hydrogen rapidly. However, no signs of reduction by the reagent were observed. It appears improbable that two molecules of such a bulky reagent could substitute for the two hydrogen atoms of the amide grouping. Consequently, we suggest that the first mole must produce the disiamylborane derivative of the tautomeric form of the amide, so that the final product contains one disiamylborane moiety on both the oxygen and nitrogen atoms (eq 5).



$$RC(=O)NH_2 \xrightarrow{Sia_2BH} RC(OBSia_2)=NH \xrightarrow{Sia_2BH} RC(OBSia_2)=NBSia_2 \qquad (5)$$

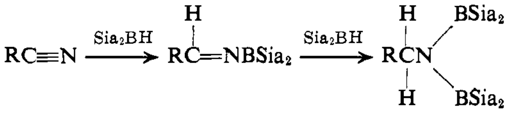
On the other hand, typical tertiary amides, such as *N*,*N*-dimethylcaproamide and *N*,*N*-dimethylbenzamide, react at a moderate rate to consume a maximum of 1 mol of hydride. This stoichiometry suggests reduction to the aldehyde stage. Indeed, hydrolysis of the intermediates produced a 72% yield of caproaldehyde and an 89% yield of benzaldehyde (eq 6). No



$$RC(=O)N(CH_3)_2 \xrightarrow{Sia_2BH} RCH(OBSia_2)N(CH_3)_2 \xrightarrow{H_2O} RCHO \qquad (6)$$

attempt was made to maximize the yields in this promising new approach to aldehydes. However, a detailed study is planned.

Finally, the rate of reaction of nitriles with the reagent proved to be very slow. However, with time the reaction proceeded beyond the uptake of one hydride, evidently involving reduction to the amine stage (eq 7). An attempt was made to control the



$$RC{\equiv}N \xrightarrow{Sia_2BH} RCH{=}NBSia_2 \xrightarrow{Sia_2BH} RCH_2N(BSia_2)_2 \qquad (7)$$

reaction to achieve the addition of only 1 mol of the reagent. Consequently, benzonitrile was permitted to react with the stoichiometric amount of reagent (1 mol/mol of nitrile) at 0° for 42 hr. However, only 9% benzaldehyde was realized after hydrolysis of the intermediate. Evidently the rate of addition of the second mole of reagent is competitive with the rate of addition of the first (eq 7).

The results of these studies of the reaction of disiamylborane with representative amides and nitrile are summarized in Table VII.

Table VII. Reaction of Disiamylborane with Representative Amides and Nitriles in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
Caproamide	1.0	1.80	1.84	0.04
	3.0	1.96	1.96	0.00
	6.0	1.96	1.96	0.00
	24.0	1.96	1.96	0.00
Benzamide	1.0	1.72	1.74	0.02
	3.0	1.89	1.90	0.01
	6.0	1.93	1.93	0.00
	24.0	1.99	1.99	0.00
N,*N*-Dimethylcaproamide	0.5	0.00	0.59	0.59
	1.0	0.00	0.71	0.71
	3.0	0.00	0.94	0.94
	6.0	0.00	1.01	1.01
	24.0	0.00	1.01	1.01
N,*N*-Dimethylbenzamide	0.5	0.00	0.68	0.68
	1.0	0.00	0.77	0.77
	3.0	0.00	1.01	1.01
	6.0	0.00	1.01	1.01
	24.0	0.00	1.01	1.01
Capronitrile	1.0	0.05	0.06	0.01
	6.0	0.05	0.06	0.01
	24.0	0.05	0.42	0.37
	72.0	0.05	1.34	1.29
Benzonitrile	1.0	0.04	0.30	0.26
	6.0	0.04	0.63	0.59
	24.0	0.04	1.33	1.29
	48.0	0.04	1.70	1.66
	72.0	0.04	1.89	1.85

[a] See Table I, footnote *a*. [b] See Table I, footnote *b*.

Nitro Compounds and Their Derivatives. 1-Nitropropane did not react with this reagent under the standard conditions. However, nitrobenzene underwent a

---

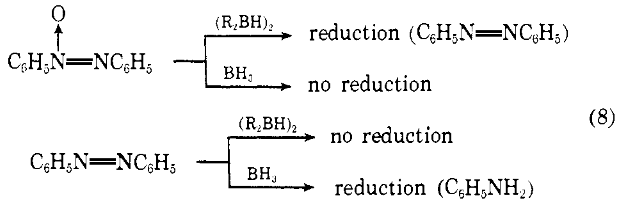
(11) Certain useful developments have been described in preliminary communications: H. C. Brown and N. M. Yoon, *J. Amer. Chem. Soc.*, 90, 2686 (1968); H. C. Brown and N. M. Yoon, *Chem. Commun.*, 1549 (1968).

Table VIII. Reaction of Disiamylborane with Nitro Compounds and Their Derivatives in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydrogen used[b]	Hydride used for reduction[b]
1-Nitropropane	3.0	0.00	0.00	0.00
	6.0	0.00	0.00	0.00
	24.0	0.00	0.00	0.00
Nitrobenzene	24.0	0.19	0.79	0.60
	48.0	0.34	1.37	1.03
	72.0	0.39	1.66	1.27
Azobenzene	0.5	0.00	0.01	0.01
	1.0	0.00	0.01	0.01
	3.0	0.00	0.01	0.01
Azoxybenzene[c]	3.0	0.37	0.76	0.39
	6.0	0.52	1.08	0.56
	12.0	0.71	1.43	0.72
	24.0	0.97	1.97	1.00
	48.0	0.97	1.97	1.00

[a] See Table I, footnote *a*. [b] See Table I, footnote *b*. [c] Solution changed from light yellow to deep orange.

slow reaction, with accompanying hydrogen evolution. Azoxybenzene was reduced slowly to the azobenzene stage, consuming two hydrides, one for hydrogen evolution and the other for reduction. Azobenzene did not react under these conditions. These results are in considerable contrast to the related reductions with diborane[5] (eq 8). The results are summarized in Table VIII.



Other Nitrogen Compounds. Cyclohexanone oxime liberated only hydrogen, with no reduction. This is again in contrast to the behavior of diborane, which not only reduces this compound to the hydroxylamine,[12] but also attacks the C=N bond in preference to the active hydrogen.[13] Phenyl isocyanate consumed two hydrides in 6 hr, similar to the behavior of diborane.

Table IX. Reaction of Disiamylborane with Other Nitrogen Compounds in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
Cyclohexanone oxime	0.5	0.73	0.74	0.01
	1.0	0.87	0.87	0.00
	3.0	1.02	1.03	0.01
	6.0	1.02	1.03	0.01
Phenyl isocyanate	0.5	0.00	0.42	0.42
	1.0	0.00	0.70	0.70
	3.0	0.00	1.44	1.44
	6.0	0.00	1.98	1.98
	24.0	0.00	1.98	1.98
Pyridine[c]	3.0	0.05	0.08	0.03
	6.0	0.05	0.08	0.03
	24.0	0.05	0.08	0.03
Pyridine *N*-oxide[c]	3.0	0.70	1.01	0.31
	6.0	0.88	1.49	0.61
	12.0	0.97	2.00	1.03
	24.0	0.97	2.00	1.03

[a] See Table I, footnote *a*. [b] See Table I, footnote *b*. [c] Refluxing concentrated hydrochloric acid was used to decompose aliquots. (Hydrolysis with the usual glycerine-water mixture proved to be very slow, requiring up to 2 hr.)

Pyridine *N*-oxide consumed two hydrides, one for hydrogen evolution and the other for reduction, presumably forming pyridine which is not further reduced under these conditions. The results are summarized in Table IX.

Sulfur Compounds. Of the sulfur compounds tested, only dimethyl sulfoxide underwent reduction, presumably to dimethyl sulfide. Two sulfonic acids, methanesulfonic acid and toluenesulfonic acid, both liberated hydrogen quantitatively. However, no reduction occurred. Disulfides, sulfide, sulfone, and tosylate were all inert. These results are very similar to those realized with diborane, previously explored.[5] The results are summarized in Table X.

Table X. Reaction of Disiamylborane with Representative Sulfur Derivatives in Tetrahydrofuran at 0°

Compound[a]	Time, hr	Hydrogen evolved[b]	Hydride used[b]	Hydride used for reduction[b]
Di-*n*-butyl disulfide	0.5	0.00	0.00	0.00
	1.0	0.00	0.03	0.03
	3.0	0.00	0.07	0.07
Diphenyl disulfide	0.5	0.00	0.00	0.00
	1.0	0.00	0.00	0.00
	3.0	0.00	0.04	0.04
Methyl *p*-tolyl sulfide	0.5	0.00	0.00	0.00
	1.0	0.00	0.00	0.00
	3.0	0.00	0.00	0.00
Dimethyl sulfoxide	1.0	0.69	1.37	0.68
	3.0	0.96	2.00	1.04
	6.0	0.96	2.00	1.04
Diphenyl sulfone	0.5	0.00	0.00	0.00
	1.0	0.00	0.00	0.00
	3.0	0.00	0.00	0.00
Methanesulfonic acid	0.5	0.99	1.03	0.04
	1.0	0.99	1.03	0.04
	3.0	0.99	1.03	0.04
p-Toluenesulfonic acid monohydrate	0.5	3.06	3.07	0.01
	1.0	3.06	3.07	0.01
	3.0	3.06	3.07	0.01
Cyclohexyl tosylate	0.5	0.00	0.00	0.00
	1.0	0.00	0.00	0.00
	3.0	0.00	0.00	0.00

[a] See Table I, footnote *a*. [b] See Table I, footnote *b*.

Synthetic Possibilities for Disiamylborane. It was previously demonstrated that disiamylborane is a highly selective hydroborating agent,[3] much more selective than diborane itself. The present study reveals that disiamylborane is likewise a highly selective reducing agent. It is desirable at this point to indicate the most promising areas of possible application.

Disiamylborane reacts rapidly with the less hindered hydroxyl groups of alcohols, but much more sluggishly with highly hindered tertiary alcohols. This suggests the use of disiamylborane to react preferentially with the primary hydroxyl group of a polyol containing secondary and/or tertiary hydroxyl groups. In this way the secondary and/or tertiary hydroxyl groups can be operated upon by suitable reactions, such as acylation, while the primary hydroxyl group is protected.

---

(12) H. Feuer, B. F. Vincent, Jr., and R. S. Bartlett, *J. Org. Chem.*, **30**, 2877 (1965).

(13) S. L. Ioffe, V. A. Tartakovskii, A. A. Medvedeva, and S. S. Novikov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1537 (1964).

Simple oxidation by alkaline hydrogen peroxide then liberates the primary hydroxyl.[14]

Disiamylborane reduces aldehydes and ketones rapidly and efficiently. Consequently, it permits the ready reduction of such groups in the presence of many other substituents, such as carboxylic acids, carboxylic acid esters, nitriles, nitro, and many of the sulfur groups examined. Of course, sodium borohydride exhibits a similar selectivity. However, the latter reagent cannot be utilized for the selective reduction of the carbonyl group of aldehydes and ketones in the presence of the acid chloride group or the carboxylic acid group, whereas disiamylborane should be applicable for such selective reductions. Disiamylborane should be especially useful for the selective reduction of aldehydes and ketones in the presence of reactive halogen substituents. More generally, it should be useful in instances where it is desirable to avoid the alkaline conditions inherent in the application of sodium borohydride.

The large steric requirements of disiamylborane make it especially effective in cases where one wishes to achieve steric control of the direction of reduction of cyclic ketones. Indeed, it has been suggested that such dialkylboranes are especially valuable in providing consistent steric control of reduction in both flexible monocyclic and in rigid bicyclic systems.[4c]

The relatively rapid reaction of disiamylborane with lactones to provide a convenient entry to the corresponding hydroxyaldehydes represents another highly promising area. Indeed, a considerable number of interesting applications of the reagent for this purpose have already been described.[9]

The reduction of tertiary amides to aldehydes represents another promising area of application. Although this reduction is readily achieved with lithium triethoxyaluminohydride,[15] disiamylborane is a less active, less basic reducing agent which should prove useful in special situations requiring such characteristics.

The apparently simple reduction of the azoxy grouping and of the pyridine *N*-oxide grouping represents other areas which should be further explored.

However, it would appear that the most important application of disiamylborane is its use for the selective hydroboration of carbon–carbon double and triple bonds in the presence of a wide variety of functional groups. Thus there is no difficulty in achieving the conversion of 10-undecenoic acid, the corresponding ester or nitrile to the hydroboration product without reduction of the functional group. Only in the case of the highly reactive aldehyde grouping and some of the more reactive ketones should one anticipate competitive reduction accompanying the hydroboration of terminal double bonds and either terminal or internal triple bonds. Of course, the rates of hydroboration of the more inert highly substituted internal double bonds are relatively slow.[3] Consequently, in such cases the situation will be complicated by the competitive reduction of some of the other, less reactive functional groups.

Comparison of Disiamylborane and Diborane. Interesting similarities and differences are apparent in the properties of the two reagents.

Although diborane is dimeric in the gaseous state and in inert solvents, it is monomeric in tetrahydrofuran.[16] It is believed that tetrahydrofuran is sufficiently basic to form a typical addition compound, $(CH_2)_4O \cdot BH_3$.

On the other hand, disiamylborane exists in tetrahydrofuran as the dimer.[17] Evidently the large steric requirements of the siamyl groups hinder coordination of the disiamylborane moiety with the cyclic ether, so that dissociation fails to occur.

The effect of the large steric requirements of the siamyl groups appears to be responsible for a large part of the observed differences in the behavior of the two reagents. For example, diborane reacts readily to liberate hydrogen with alcohols, even alcohols which are highly hindered. On the other hand, disiamylborane fails to react under the standard conditions with the more hindered alcohols, such as 3-ethyl-3-pentanol.

Possibly related is the observation that thiols react with borane to liberate hydrogen, whereas such thiols are inert to disiamylborane. Both the reactions of alcohols and those of thiols with these reagents are believed to proceed through a prior coordination of the boron atom with a lone pair of the oxygen or sulfur atom,[5] and the siamyl groups would interfere seriously with such a donor–acceptor interaction.

Somewhat surprising is the observation that phenol liberates 1 equiv of hydrogen in 12 hr with borane, but requires only 0.5 hr with disiamylborane. Clearly the latter reaction must not involve prior coordination. The inductive effect of the two siamyl groups must increase the hydridic character of the hydrogen atom in disiamylborane, as compared to borane, so that this reaction may involve a direct attack by the acidic proton.

Disiamylborane readily reacts with carboxylic acids to liberate hydrogen and form the anhydride of disiamylborinic acid and the carboxylic acid. However, the product is stable to further attack by disiamylborane, presumably a consequence of the large steric requirements of the reagent. On the other hand, borane reacts with 3 mol of the carboxylic acid to produce the triacycloxyborane, $(RCO_2)_3B$, and the latter is rapidly attacked by additional borane to produce the alcohol (after hydrolysis).[5]

Again the reaction of disiamylborane with lactones is readily controlled to achieve the partial reduction to the hydroxyaldehyde. However, the corresponding reduction with borane goes rapidly past this stage to yield the diol predominantly.

Tertiary amides react with only 1 mol of disiamylborane and the reaction essentially stops at that stage. Hydrolysis of the intermediate yields the corresponding aldehyde. On the other hand, the reduction with borane proceeds rapidly to the amine stage and it proved impossible to halt the reaction at the intermediate stage.[18]

The nitro group is essentially inert to borane under the standard conditions. However, nitrobenzene is slowly reduced, with hydrogen evolution, by disiamylborane. Moreover, the reactions of azobenzene

---

[14] Preliminary experiments of this kind with Dr. D. B. Bigley have been quite promising.

[15] H. C. Brown and A. Tsukamoto, *J. Amer. Chem. Soc.*, 86, 1089 (1964).

[16] B. Rice, J. A. Livasy, and G. W. Schaeffer, *J. Amer. Chem. Soc.*, 77, 2750 (1955).

[17] H. C. Brown and G. J. Klender, *Inorg. Chem.*, **1**, 204 (1962).

[18] H. C. Brown and P. Heim, *J. Amer. Chem. Soc.*, **86**, 3566 (1964).

and azoxybenzene are quite different with these two reagents. Thus, under the standard conditions, borane reacts only with the former, whereas disiamylborane reacts only with the latter.

Finally, cyclohexanone oxime is readily reduced to hydroxylamine by borane, whereas disiamylborane reacts to liberate hydrogen, but no reduction of the oxime grouping occurs under the standard condition.

It is evident that this discussion can only skim the surface of the many interesting reactions exhibited by disiamylborane and its many similarities and differences to borane. More detailed studies of many of these features are required to achieve a fuller understanding.

Experimental Section

Materials. The compounds used were from the same collection used in the earlier studies.[5,6] The standard solutions of diborane were prepared following the procedure described previously,[19] only changing the order of addition. That is, we added boron trifluoride etherate to the slurry of sodium borohydride in diglyme. The diborane generated was washed with saturated sodium borohydride solution in diglyme.

Standard Solution of Disiamylborane. A 500-ml flask equipped with a Dry Ice condenser, connected to a gas meter and an inlet tube, was placed in ice–salt mixture bath (−10°) and maintained under dry nitrogen as the apparatus was cooled. To this flask there was introduced 211 ml of 1.48 *M* borane solution (312 mmol of borane). Then 43.75 g of 2-methyl-2-butene (625 mmol) was added slowly by means of a hypodermic syringe, dipping the syringe needle into the borane solution, as the solution was vigorously stirred with a magnetic stirrer. The addition was completed in 30–60 min and the stirring was continued for an additional 1 or 2 hr.

The reaction mixture was allowed to stand overnight in a cold room (−10°). Analysis revealed that the hydride concentration was 1.22 *M*, as measured volumetrically.

Stability of Disiamylborane Solution in Tetrahydrofuran (THF). The stability of disiamylborane solution in THF was examined by following the change in hydride concentration with time at 25, 50, and 65° (refluxing THF). The results are summarized in Table XI.

Table XI. The Stability of Disiamylborane in Tetrahydrofuran at Various Temperatures

Temp, °C	Time, hr[a]							
	0	0.5	1.0	3.0	6.0	12.0	24.0	48.0
25	1.02	1			1.02 (100)		0.96 (94)	1.05 (103)
50	1.07		1.94 (97)	1.02 (96)	1.04 (97)	1.04 (97)	0.98 (92)	
65	1.10		1.07 (97)	1.06 (96)	1.05 (95)	1.03 (94)	1.06 (96)	

[a] The figures give the change in hydride concentration with time (*M*). The figures in parentheses give the per cent of the initial value.

Behavior of the Tetrahydrofuran Solution of Disiamylborane toward Air. A standard solution of disiamylborane in THF (approximately 1.0 *M*) was prepared and subjected to the following tests at room temperature.

1. A 5-ml sample of the above solution was removed with a syringe and discharged through air into an evaporating dish. The solution did not catch fire, indicating the solution is not spontaneously inflammable.
2. A 5-ml sample of the above solution was placed in an evaporating dish and allowed to stand exposed to the open air. Gas evolution was observed and the solution became warm. As the gas bubbles disappeared (~5 min), the solution cooled down. After 3 hr, a white solid remained which contained no hydride.
3. A flask and a condenser (protected by a drying tube) was flushed with dry air. Then 30 ml of a standard solution (1.00 *M*) was introduced into the flask and allowed to stand exposed to the dry air with constant stirring at room temperature.

Aliquots were removed and analyzed for residual hydride. The observed decrease in the hydride concentration is summarized in Table XII.

Table XII. Loss of Hydride from Disiamylborane Solution in Tetrahydrofuran in the Presence of Air at Room Temperature

	Time, hr							
	0	0.5	1.0	3.0	6.0	12.0	24.0	48.0
M in hydride	1.00	0.99	0.99	0.95	0.89	0.83	0.77	0.52
% H^-	(100)	(99)	(99)	(95)	(89)	(83)	(77)	(52)

Procedure for Rate and Stoichiometry Studies. The reaction of *N*,*N*-dimethylbenzamide is described as representative. A 100-ml hot, dry reaction flask, equipped with inlet tube and reflux condenser connected to gas meter *via* a Dry Ice trap, was placed in an ice bath and cooled down under dry nitrogen. In this flask, 11 ml of 1.82 *M* disiamylborane (20 mmol in hydride) and 4 ml of THF were placed, and 0.746 g (5 mmol) of *N*,*N*-dimethylbenzamide dissolved in 5 ml of THF at 0° was introduced by means of a hypodermic syringe. No hydrogen evolution was observed. After 30 min, 4 ml of the reaction mixture (corresponding to 1 mmol of compound) was withdrawn by hypodermic syringe and hydrolyzed with a 1:1 mixture of glycerine and water. There was obtained 3.30 mmol of hydrogen, whereas 4 ml of a blank solution gave 3.98 mmol of hydrogen. Therefore 0.68 mmol of hydride (3.98–3.30) was consumed/mmol of compound. The residual hydride per millimole of compound was 3.21 mmol after 1 hr and 2.97 mmol after 3 hr. These correspond to 0.77 and 1.01 mmol of hydride uptake for the corresponding reaction times. The residual hydride remained constant, 2.97 mmol after 6 hr, showing no further reaction. In another run, the reaction time was extended to 12 and 24 hr at 0°. However, no changes in residual hydride were observed.

Reduction of *N*,*N*-Dimethylbenzamide to Benzaldehyde. To a 30-mmol sample of disiamylborane (in hydride) in 50 ml of THF, there was added 4.47 g (30 mmol) of *N*,*N*-dimethylbenzamide, dissolved in 10 ml of THF at room temperature. The reaction was followed by glpc analysis on a 5-ft silicon oil column at 200° after destroying excess hydride with 1-octene. *n*-Dodecane was used as an internal standard. After 41 hr, 87% *N*,*N*-dimethylbenzamide had been consumed. After hydrolysis, glpc analysis revealed a 78% yield of benzaldehyde. Correcting for the fact that the reaction had not yet gone to completion, the yield is 89%.

Hydrolysis of a Difficultly Hydrolyzable Reaction Mixture. In the reaction involving *n*-hexylamine, we observed that the residual hydride could not be obtained with the usual 1:1 mixture of glycerine and water. Presumably, the addition compound, *n*-hexylaminedisiamylborane is stable to this medium. This difficulty was overcome by using concentrated hydrochloric acid at refluxing temperature. This altered hydrolytic procedure was also utilized for the reaction of pyridine and for others which produce intermediates (nitrogen derivatives) difficult to hydrolyze.

Reduction of γ-Butyrolactone to γ-Hydroxybutyroaldehyde. To 30 mmol of disiamylborane in 50 ml of THF there was added 2.58 g (30 mmol) of γ-butyrolactone dissolved in 10 ml of THF at 0°. The reaction was followed by glpc analysis, after destroying excess hydride with 1-octene. After 44 hr at 0°, 85% lactone had reacted. A 20-ml aliquot of the above reaction mixture (10 mmol of compound) was added to 1 l. of 2,4-dinitrophenylhydrazine reagent (2 *N* HCl). After standing 12 hr at 0°, the precipitate was filtered and washed. The crude precipitate (1.92 g, mp 105–112°) was recrystallized from ethanol. There was obtained 1.68 g of γ-hydroxybutyraldehyde-2,4-dinitrophenylhydrazone, mp 114–117° (overall yield 74%). After another recrystallization from ethanol, the product exhibited mp 117–118°.

---

(19) G. Zweifel and H. C. Brown, *Org. React.*, 13, 1 (1963).