# Reaction of Sodium Aluminum Hydride with Selected Organic Compounds Containing Representative Functional Groups. Comparison of the Reducing Characteristics of Lithium and Sodium Aluminum Hydrides

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The approximate rate and stoichiometry of the reaction of excess sodium aluminum hydride (SAH) with organic compounds containing representative functional groups under standardized conditions (tetrahydrofuran, 0 °C) were examined in order to define the reducing characteristics of the reagent and compare the reducing power with lithium aluminum hydride (LAH). In general, the reducing action and power of the reagent are similar to those of LAH. All of the active hydrogen compounds including alcohols, amines, and thiols evolve hydrogen instantly. Aldehydes and ketones are reduced very rapidly and quantitatively to give the corresponding alcohols. Unlike LAH, SAH reduces carboxylic acids and their salts only slowly to the corresponding alcohols. Similarly, anhydrides are reduced slowly to the diols. Acid chlorides, esters, and lactones consume 2 equiv of hydride in less than 15 min at 0 °C to give the corresponding alcohols. However, the reaction of epoxides with this reagent proceeds at a much slower rate than LAH, requiring 6–24 h at 0 °C and 1–6 h at room temperature. Both primary aliphatic and aromatic amides examined evolve 2 equiv of hydrogen rapidly and are reduced slowly to the alcohols. Tertiary amides rapidly utilize 2 equiv of hydride for reduction. The reaction of tertiary amides with a limiting amount of the reagent provides the aldehydes in yields of around 80%. Benzonitrile also readily reacts to give the amine, while the reaction of capronitrile liberates *ca.* 0.4 equiv of hydrogen and consumes less than 2 equiv of hydride for reduction both at 0 °C and room temperature. Aromatic nitro compounds examined also undergo the reaction readily to give the hydrazobenzene derivatives similar to the case with LAH. Oximes, phenyl isocyanate, disulfides, and sulfoxides are also readily reduced, while sulfides, sulfones, and tosylates are inert to this reagent. Finally, the similarities and differences in the reaction of organic compounds with LAH and SAH are established in this study.

Since Finholt and co-workers reported that lithium and sodium aluminum hydrides are essentially equivalents as reducing agents,[1] a number of interesting papers utilizing sodium aluminum hydride (SAH) for reduction of organic and nonorganic functional compounds have been published.[2] However, most of the reduction data available are for preparative purposes; they do not show any actual differences on reducing action toward the general organic compounds between LAH and SAH, although Ashby and his co-workers have reported that LAH is about 10 times more reactive than SAH in the reduction of ketones.[3]

Consequently, in order to compare the reducing characteristics of these two aluminum hydrides,[4] we undertook a systematic study of the rate and stoichiometry of the reaction of SAH with organic compounds containing representative functional groups under standardized conditions.

## Results and Discussion

**Preparation of a Standard Solution of Sodium Aluminum Hydride (SAH).** A standard solution of SAH in THF was prepared by adding an appropriate amount of solvent onto a powder of SAH and stirring the resulting slurry for 48 h. Standardization of the clear and colorless solution of SAH by sodium, aluminum, and gas evolution analysis confirmed that the ratio of Na/Al/H is 1/1/4. Also, $^{27}$Al NMR of SAH in THF showed a clean, sharp quintet ($J_{Al-H}$ = 175 Hz) centered at $\delta$ +96.7 ppm relative to $[Al(H_2O)_6]^{3+}$.

**Procedure for Rate and Stoichiometry Studies.** The general procedure involved preparation of a reaction mixture of sodium aluminum hydride (0.25 M, 1.00 M in hydride) and the compound (0.25 M) in tetrahydrofuran (THF) at 0 °C. Hydrogen evolution following addition of the compound to the reagent solution was measured. A blank reaction was run under identical conditions but without addition of the compound. From time to time, aliquots were taken from the reaction mixture and analyzed for the remaining hydride by hydrolysis. From the difference in yields of hydrogen in the two cases, the hydride utilized by the compound for reduction was calculated. In this manner, the number of moles of hydride used by compound for hydrogen formation and the number of moles of utilized for reduction were determined.

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(3) Ashby, E. C.; Boone, J. R. *J. Am. Chem. Soc.* **1976**, *98*, 5524.

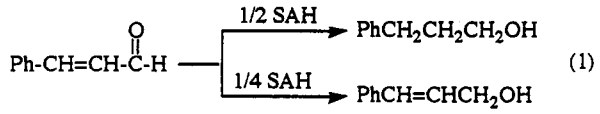
(4) Brown, H. C.; Weissman, P. M.; Yoon, N. M. *J. Am. Chem. Soc.* **1966**, *88*, 1458.

0022-3263/93/1958-4727$04.00/0 

In cases where the compound consumes more than 3 equiv of hydride, the hydride concentration was maintained at a constant, but the concentration of compound was reduced to give a higher ratio. In some cases where the reaction did not come to an expected stoichiometry at 0 °C, the reaction was reported at room temperature.

**Alcohols, Phenols, Amines, and Thiols (Active Hydrogen Compounds).** All of the active hydrogen compounds examined evolved 1 molar equiv of hydrogen immediately at 0 °C. Therefore, no difference in reactivity toward the active hydrogen compounds between LAH[4] and SAH is observed in this study. These results are summarized in Table I.

**Aldehydes and Ketones.** Like LAH, the reagent SAH reduced all of the saturated aldehydes and ketones examined to the corresponding alcohols within 5 min at 0 °C. Cinnamaldehyde, an $\alpha,\beta$-unsaturated aldehyde, utilized 2 equiv of hydride rapidly, indicating rapid involvement of the double bond. In fact, the reaction yields 100% of hydrocinnamyl alcohol without any detection of $\alpha,\beta$-unsaturated alcohol. However, when 0.25 equiv of SAH was added to the solution of compound (*i.e.*, inverse addition) at 0 °C, cinnamyl alcohol was produced exclusively (eq 1). LAH also attacks the double bond of



(1)

cinnamaldehyde to yield hydrocinnamyl alcohol. The reduction of norcamphor under these conditions provides 88% *endo*- and 12% *exo*-norborneol, showing a similar stereoselectivity to that with LAH (*i.e.*, *endo*:*exo* = 90:10).[5] These results are summarized in Table I.

**Quinones.** Both *p*-benzoquinone and anthraquinone readily consumed 2 equiv of hydride per mole of compound, of which *ca.* 40% was utilized for hydrogen evolution and the remaining *ca.* 60% for reduction, with an accompanying color change to yellow. A similar result from LAH, but a different ratio of hydride consumption for hydrogen evolution and reduction, was realized. These data indicate that the reduction dose not involve simple reduction either to aromatic diol or to 1,4-reduction product. The experimental data are summarized in Table I.

**Carboxylic Acid and Acyl Derivatives.** Carboxylic acids instantly evolve 1 equiv of hydrogen and form a gel-like precipitate. The subsequent reduction proceeded slowly, requiring 2 days for reduction to the alcohols at 0 °C. Apparently this much slower reduction compared to the relatively fast reaction with LAH (6 h) is due to the low solubility of precipitate. However, warming the reaction to room temperature accelerated the rate of reaction, showing the complete reduction in 6 h.

The reagent, SAH, also reduced sodium caproate to the corresponding alcohol in 48 h at 0 °C and 12 h at room temperature. On the other hand, sodium benzoate was essentially inert to the reagent at 0 °C but slowly reduced to the corresponding alcohol in 3 days at room temperature.

In the case of anhydrides, the rate of reduction with SAH is slower than that with LAH, requiring 2–3 days for completion at 0 °C. However, all of the anhydrides examined are reduced to the corresponding diols at room temperature in 6–24 h. This relative slower reaction of SAH may be attributed to the low solubility of sodium carboxylate derivative in the solvent. On the contrary, SAH reduced acid chlorides examined at a faster rate than with LAH,[4] showing complete reduction to the alcohols within 15 min at 0 °C. These results are summarized in Table I.

**Esters and Lactones.** All of the esters and lactones examined in this study are reduced rapidly with the uptake of 2 equiv of hydride to give quantitative yields of the corresponding alcohols, which are similar to the cases with LAH[4] except for isopropenyl acetate. In the case of isopropenyl acetate, different stoichiometries are realized. Thus, LAH reduction utilized a total of 3 equiv of hydride, indicating involvement on the double bond,[4] whereas SAH reduction did not show any further hydride uptake beyond 2 equiv, even for a long reaction time (24 h). These results are summarized in Table I.

**Epoxides.** The reaction of SAH with epoxides examined proved much slower than that of LAH, requiring 6–24 h at 0 °C to consume 1 equiv of hydride and 1–6 h at room temperature. From this considerable rate difference, one can assume the role of cation in the step for epoxy ring opening. Lithium cation can coordinate on the epoxy oxygen effectively to assist the carbon–oxygen bond breaking.

However, the selectivity toward unsymmetrical epoxides appeared to be quite similar to LAH,[4] showing the major hydride transfer to the less substituted carbon atom of the epoxy ring. Thus, 1,2-butylene oxide and 1-methyl-1,2-cyclohexene oxide yielded 100% of the secondary and tertiary alcohols, respectively. In the case of styrene oxide, 97% of 1-phenylethanol, the secondary alcohol, and 3% of 2-phenylethanol, the primary alcohol, were produced at 0 °C. These results are summarized in Table I.

**Amides and Nitriles.** Primary amides, such as caproamide and benzamide, evolved 2 equiv of hydrogen within 5 min at 0 °C with no significant difference in the first and second equiv of hydrogen formation. However, in both cases, the reduction proceeded only sluggishly at 0 °C with formation of precipitate as the reaction proceeded. Even at room temperature, reaction for 24 h was required to take up 2 equiv of hydride for the formation of the corresponding amines. No significant rate difference in the reduction of primary amides with SAH and LAH was realized.

On the other hand, tertiary amides reacted readily with this reagent with the uptake of 2 equiv of hydride in 3 h at 0 °C. Finally, nitriles utilized approximately 2 equiv of hydride for reduction at a relatively fast rate, both at 0 °C and room temperature. These results are summarized in Table I.

Two decades ago Zakharkin and co-workers established a general procedure for the preparation of aldehydes from *N,N*-dimethylamides with a limiting amount of SAH at room temperature in yields of from 70% to 90%.[2d] They also pointed out that the mode of reagent addition and a molar ratio of the reagent to amide vary the reaction products significantly. In the present study we confirmed that this reagent is excellent for the transformation of tertiary amides to aldehydes. Thus, reaction by addition of 0.25 equiv of reagent to the tertiary caproamide yielded 86% of caproaldehyde at 0 °C and 77% at room temperature, both analyzed by (2,4-dinitrophenyl)hydrazine (eq 2). On the other hand, GC analysis revealed that

$$RC(O)NMe_2 \xrightarrow[0\ ^\circ C\ or\ rt]{1/4\ SAH} RCHO \qquad (2)$$

(5) Hermanek, S.; Kriz, O.; Plesek, J.; Hanslik, T. *Chem. Ind.* **1975**, 42.

**Table I. Reaction of Representative Organic Derivatives with Excess Lithium Aluminum Hydride and Sodium Aluminum Hydride in Tetrahydrofuran at 0 °C**

| | $LiAlH_4$ | | | $NaAlH_4$ | | |
|---|---|---|---|---|---|---|
| compd[a] | time, h | $H_2$ evoln | hydride used for rdn | time, h | $H_2$ evoln | hydride used for rdn |
| **I. Active Hydrogen Compounds** | | | | | | |
| 1-hexanol | 5 min[b] | 1.00 | 0.00 | 5 min | 1.01 | 0.00 |
| benzyl alcohol | 5 min[b] | 1.00 | 0.00 | 5 min | 0.99 | 0.00 |
| 3-hexanol | 5 min[b] | 0.99 | 0.00 | 5 min | 1.03 | 0.00 |
| 3-ethyl-3-pentanol | 5 min[b] | 1.00 | 0.00 | 5 min | 1.02 | 0.00 |
| phenol | 5 min[b] | 1.00 | 0.00 | 5 min | 0.99 | 0.00 |
| *n*-hexylamine | 0.25[b] | 2.00 | 0.00 | 0.25 | 2.00 | 0.00 |
| 1-hexanethiol | 5 min[b] | 0.99 | 0.00 | 5 min | 0.99 | 0.00 |
| benzenethiol | 5 min[b] | 1.01 | 0.00 | 5 min | 1.01 | 0.00 |
| **II. Aldehydes and Ketones** | | | | | | |
| caproaldehyde | 0.5 | 0.04 | 1.02 | 5 min | 0.01 | 1.01 |
| benzaldehyde | 0.5 | 0.11 | 0.96 | 5 min | 0.02 | 1.00 |
| 2-heptanone | 0.5 | 0.09 | 1.01 | 5 min | 0.00 | 1.01 |
| norcamphor | 5 min[b] | 0.00 | 1.01 | 5 min | 0.01 | 0.99 |
| acetophenone | 0.5 | 0.04 | 1.04 | 5 min | 0.00 | 0.99 |
| benzophenone | 5 min[b] | 0.01 | 1.00 | 5 min | 0.01 | 1.00 |
| **III. Quinones** | | | | | | |
| *p*-benzoquinone | 1.0 | 0.58 | 1.20 | 6.0 | 0.81 | 1.20 |
| anthraquinone | 6.0 | 0.24 | 1.81 | 12.0 | 0.84 | 1.20 |
| **IV. Carboxylic Acids and Acyl Derivatives** | | | | | | |
| caproic acid | 6.0 | 1.05 | 1.95 | 48.0 | 1.04 | 2.01 |
| benzoic acid | 6.0 | 1.01 | 1.99 | 48.0 | 1.02 | 2.02 |
| acetic anhydride[c] | 3.0 | 0.17 | 4.01 | 6.0[d] | 0.03 | 4.02 |
| succinic anhydride[c] | 24.0 | 0.06 | 3.76 | 24.0[d] | 0.05 | 4.03 |
| phthalic anhydride[c] | 12.0 | 0.00 | 3.74 | 48.0 | 0.04 | 3.97 |
| caproyl chloride | 0.5 | 0.00 | 1.97 | 0.25 | 0.01 | 2.01 |
| benzoyl chloride | 0.5 | 0.00 | 1.97 | 0.25 | 0.02 | 2.00 |
| **V. Esters and Lactones** | | | | | | |
| ethyl caproate | 0.5 | 0.04 | 2.03 | 0.5 | 0.00 | 1.99 |
| ethyl benzoate | 0.5 | 0.08 | 1.97 | 0.5 | 0.01 | 2.00 |
| phenyl acetate | 0.5 | 0.05 | 1.99 | 5 min | 0.00 | 2.00 |
| γ-butyrolactone | 0.5 | 0.04 | 2.13 | 5 min | 0.00 | 2.01 |
| phthalide | 0.5 | 0.00 | 1.99 | 0.25 | 0.01 | 2.00 |
| isopropenyl acetate | 24.0 | 0.10 | 2.95 | 1.0 | 0.00 | 2.01 |
| **VI. Epoxides** | | | | | | |
| 1,2-butylene oxide | 1.0 | 0.00 | 1.02 | 24.0 | 0.00 | 1.01 |
| styrene oxide | 0.5 | 0.02 | 1.00 | 6.0 | 0.01 | 1.01 |
| cyclohexene oxide | 1.0 | 0.04 | 0.96 | 6.0 | 0.01 | 1.02 |
| 1-methyl-1,2-cyclohexene oxide | 1.0 | 0.04 | 0.96 | 24.0 | 0.00 | 0.99 |
| **VII. Amides and Nitriles** | | | | | | |
| carpoamide[c] | 6.0[d] | 2.01 | 2.01 | 12.0[d] | 2.04 | 1.98 |
| benzamide[c] | 3.0[d] | 2.20 | 2.07 | 24.0[d] | 2.01 | 2.01 |
| *N,N*-dimethylcaproamide | 3.0 | 0.03 | 1.98 | 3.0 | 0.00 | 1.99 |
| *N,N*-dimethylbenzamide | 3.0 | 0.00 | 2.02 | 3.0 | 0.01 | 2.00 |
| capronitrile | 3.0 | 0.24 | 1.79 | 24.0 | 0.37 | 1.78 |
| benzonitrile | 3.0 | 0.00 | 1.94 | 6.0 | 0.01 | 2.02 |
| **VIII. Nitro Compounds and Their Derivatives** | | | | | | |
| 1-nitropropane[e] | 48.0[d] | 2.92 | 3.05 | 1.0[d] | 3.01 | 2.98 |
| nitrobenzene[e] | 3.0 | 2.53 | 2.53 | 24.0 | 2.53 | 2.52 |
| azobenzene | 3.0[d,f] | 0.99 | 1.06 | 6.0[c,d] | 1.03 | 1.02 |
| azoxybenzene | 3.0[f] | 1.99 | 2.05 | 24.0[c] | 1.99 | 2.00 |
| **IX. Other Nitrogen Compounds** | | | | | | |
| cyclohexanone oxime[c] | 6.0[d] | 1.87 | 1.82 | 48.0[d] | 2.02 | 1.98 |
| phenyl isocyanate | 24.0 | 0.04 | 2.99 | 1.0 | 0.02 | 3.01 |
| pyridine | 3.0[d] | 0.06 | 0.12 | 48.0[d] | 0.02 | 0.13 |
| 4-picoline *N*-oxide | 1.0 | 0.34 | 1.93 | 6.0 | 0.09 | 1.98 |
| **X. Sulfur Compounds** | | | | | | |
| di-*n*-butyl disulfide | 1.0 | 0.98 | 1.01 | 3.0 | 1.00 | 1.00 |
| diphenyl disulfide | 0.5 | 1.01 | 1.00 | 0.25 | 1.03 | 1.01 |
| phenyl *n*-propyl sulfide | 24.0 | 0.00 | 0.20 | 24.0[d] | 0.00 | 0.00 |
| dimethyl sulfoxide | 6.0 | 1.12 | 0.94 | 24.0 | 1.02 | 0.98 |
| diphenyl sulfone | 24.0[d] | 0.02 | 0.29 | 24.0[d] | 0.01 | 0.10 |
| methanesulfonic acid | 3.0[d] | 1.14 | 0.01 | 6.0[d] | 1.03 | 0.01 |
| *p*-toluenesulfonic acid monohydrate[c] | 24.0[d] | 3.10 | 0.10 | 24.0[d] | 2.99 | 0.03 |
| cyclohexyl tosylate | 24.0[d] | 0.28 | 0.51 | 24.0[d] | 0.08 | 0.16 |

[a] Hydride to compound ratio 4:1, except where otherwise indicated. [b] Present study. [c] Hydride to compound ratio 6:1. [d] At room temperature. [e] Hydride to compound ratio 10:1. [f] Hydride to compound ratio 8:1.

reaction with a regular order of reagent addition and a molar ratio of SAH to the amide of 0.5 at 0 °C forms a mixture of 47% of 1-hexanol and 53% of the tertiary amide as well as a small amount of hexanal upon hydrolysis.

In the case of capronitrile, *ca.* 0.4 equiv of hydrogen was evolved immediately, both at 0 °C and room temperature, presumably by reaction of the reagent with the active α-hydrogen of the nitrile. The subsequent hydride utilization for reduction was less than 2 by approximately this amount. LAH also partially evolves hydrogen (0.24 equiv at 0 °C), but the quantity of hydrogen is smaller than that by SAH (0.37 equiv at 0 °C). However, benzonitrile was readily transformed to benzaldehyde by this reagent with a limiting amount of hydride and a reverse mode of addition at room temperature in a yield of 90%, similar to the results obtained from LAH.[6]

**Nitro Compounds and Their Derivatives.** The reagent showed the same trends in the reaction of nitro compounds examined as LAH.[4] Thus, 1-nitropropane consumed a total of 6 equiv of hydride with 3 equiv of hydride being utilized for reduction and 3 equiv for hydrogen evolution, corresponding to expected stoichiometry for reduction to the amine. It also showed rapid reduction to the hydrazo stage with a slower rupture of the nitrogen–nitrogen bond to form the amine. Nitrobenzene also reacted quite rapidly with the uptake of 5 equiv of hydride, corresponding to the formation of a hydrazobenzene derivative, and no further utilization of hydride was realized. Indeed, we isolated hydrazobenzene in a yield of 85% in a 24-h reaction time at room temperature. It is interesting to point out that Finholt isolated azobenzene from the reduction of nitrobenzene with an insufficient amount of SAH in a yield of 78%.[1] Therefore, we can conclude that nitro compounds undergo the reaction through azo and hydrazo intermediates to the final amine stage (eq 3).

$$RNO_2 \rightarrow [RN{=}NR] \rightarrow [RNHNHR] \rightarrow RNH_2 \quad (3)$$

Azobenzene utilized 2 equiv of hydride in 24 h at 0 °C and 6 h at room temperature, 1 equiv for reduction and 1 for hydrogen evolution, corresponding to the formation of a hydrazobenzene derivative. Even extending the reaction time to 24 h at room temperature did not increase the hydride utilization. This indicates that the nitrogen–nitrogen bond in a hydrazobenzene moiety is inert to this reagent under these reaction conditions. Similarly, the reagent reacted readily with azoxybenzene with the uptake of 4 equiv of hydride, 2 equiv being used for reduction and 2 for hydrogen evolution, both at 0 °C and room temperature. This stoichiometry indicates that azoxybenzene is reduced to hydrazobenzene. These results are summarized in Table I.

**Other Nitrogen Compounds.** The reaction of cyclohexanone oxime utilized 1 equiv of hydride for reduction and 1 equiv for hydrogen evolution at a relatively fast rate, followed by the slow utilization of 1 equiv of hydride for reduction and the slow liberation of a second equiv of hydrogen, corresponding to the formation of cyclohexylamine, similar to the case with LAH.[4] Interestingly, phenyl isocyanate underwent reaction readily with this reagent to utilize 3 equiv of hydride in 1 h, both at 0 °C and room temperature. LAH can reduce the compound only slowly, requiring 24 h for completion.[4] Pyridine was essentially inert to this reagent, while 4-picoline *N*-oxide utilized 2 equiv of hydride readily for reduction with the partial liberation of hydrogen. These results are summarized in Table I.

(6) Brown, H. C.; Shoaf, C. J. *J. Am. Chem. Soc.* **1964**, *86*, 1079.

**Sulfur Derivatives.** Both disulfides examined reacted rapidly with this reagent to utilize 2 equiv of hydride, 1 equiv for reduction and the second for hydrogen evolution, corresponding to the formation of 2 mol of thiol per mole of disulfide. On the other hand, sulfides proved stable to the reagent under experimental conditions. Dimethyl sulfoxide evolved 1 equiv of hydrogen readily with the slow uptake of 1 equiv of hydride for reduction to the sulfide. Diphenyl sulfone was stable even at room temperature. Methanesulfonic acid and *p*-toluenesulfonic acid monohydrate liberated hydrogen instantly and quantitatively, but no reduction was detected. Finally, cyclohexyl tosylate reacted only very sluggishly, even at room temperature, unlike the case with LAH, which reacts slowly at that temperature.[4] These results are summarized in Table I.

**Comparison of Reducing Characteristics of Lithium and Sodium Aluminum Hydrides.** Sodium aluminum hydride (SAH) was first reported to react similarly to lithium aluminum hydride (LAH) in the reduction of some organic compounds with respect to reaction rate and product yield some 38 years ago.[1] Since then, a number of reports concerning properties,[2a,7] structure,[2a,8] and preparations[2a,9] of SAH, as well as its chemistry[2a,10] and applications[2] to the reduction of organic and inorganic compounds with comparisons to LAH, have appeared. But a systematic direct comparison is needed to compare these two reducing agents for general use in organic synthesis.

These results and the comparison study between LAH and SAH are summarized in Table I. In this table, "hydrogen evolution" and "hydride used for reduction" mean the moles of hydrogen evolved and the hydride utilization only for reduction per mole of compound under investigation. In cases where no significant reduction is observed, the values listed are for the longest period for which the observation was made. Where reaction occurs, the data are for the shortest period when essentially constant values of hydrogen evolution and hydride uptake are observed. Thus, the values do not necessarily give the maximum hydrogen evolution nor the possible hydride utilization. They merely define the point where further reduction either does not occur or proceeds so slowly as to provide a convenient stopping place for the reduction.

The data for LAH are taken from the paper published.[4] However, in cases where the period of time reported is so different that it is difficult to compare the rate of reaction effectively, we repeated the reactions.

## Conclusion

This study has clearly revealed the similarities and differences in the reducing characteristics of lithium and sodium aluminum hydrides (LAH and SAH) toward 56 selected organic compounds. In general, the reducing action of SAH is very similar to that observed previously

(7) (a) Gavrichev, K. S.; Gorbunov, V. E.; Bakum, S. I. *Neorg. Khim.* **1981**, *26*, 2039. (b) Tarasov, V. P.; Bakum, S. I.; Privalov, V. I.; Busalaev, Y. A. *Koord. Khim.* **1981**, *7*, 674.

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(9) (a) Gavrilenko, V. V.; Vinnikova, M. I.; Zakharkin, L. I. *Zh. Obshch. Khim.* **1979**, *49*, 982. (b) Shen, P.; Zhang, Y.; Chen, S.; Yuan, H.; Che, Y.; Jia, J.; Wu, S. *Huaxue Tongbao* **1984**, 25. (c) Shen, P.; Zhang, Y.; Wang, D.; Chen, S. *Huaxue Shijie* **1988**, *29*, 3.

(10) (a) Ashby, E. C.; Boone, J. R. *J. Org. Chem.* **1976**, *41*, 2890. (b) Handel, H.; Pierre, J.-L. *Tetrahedron Lett.* **1976**, 741. (c) Ashby, E. C.; Boone, J. R. *J. Am. Chem. Soc.* **1976**, *98*, 5524. (d) Wiegers, K. E.; Smith, S. G. *J. Org. Chem.* **1978**, *43*, 1126. (e) Zakharkin, L. I.; Gavrilenko, V. V. *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* **1962**, 1146.

for LAH; SAH reduced almost every organic functional group as readily as LAH does. Although SAH shows a much lower reactivity than LAH toward some functionalities, such as carboxylic acids, anhydrides, epoxides, amides, and nitro compounds, it can reach the final reduction stages readily at room temperature. Such a relatively slow reaction, on the other hand, adds an advantage to SAH to show a possible selective reduction between some organic functional groups. As a consequence, SAH can replace LAH effectively in most organic reductions.

## Experimental Section

**General.** The reaction flasks and other glassware used in the experiments were predried at 140 °C for several hours, assembled hot, and cooled under a stream of nitrogen. Syringes were cooled under a stream of nitrogen and assembled. All reactions were carried out under a static pressure of nitrogen in flasks fitted with septem-covered side arms with use of standard techniques for handling air-sensitive material.[11]

The standard list of compounds examined was essentially the same as that utilized in our earlier studies. Tetrahydrofuran (THF) was distilled from sodium–benzophenone ketyl and stored under dry nitrogen. Sodium aluminum hydride (SAH) was obtained from Ethyl Corp. and used directly without further purification.

Gas chromatographic analysis for alcohol products were carried out using a gas chromatograph equipped with 12 ft × 0.125 in column of 10% Carbowax 20 M on 100–200-mesh Supelcoport. Other compounds were analyzed with use of a 12-ft × 0.125-in. column of 10% SE-30 on a 100–120-mesh Supelcoport. All GC yields were determined with use of a suitable internal standard and authentic mixture.

**Preparation of Sodium Aluminum Hydride (SAH) in Tetrahydrofuran.** An oven-dried, 2-L, round-bottom flask with side arm equipped with a magnetic stirring bar and an adaptor was attached to a mercury bubbler. The flask was flushed with dry nitrogen and then maintained under a static pressure of nitrogen. To this flask were added 27 g of SAH (500 mmol) and 1.1 L of THF. The slurry was stirred for 48 h at room temperature and then allowed to stand at 0 °C to permit the undissolved materials to settle.[12] The $^{27}Al$ NMR spectrum of the resulting clear solution showed a clean quintet centered at $\delta$ +96.7 (relative to $[Al(H_2O)_6]^{3+}$) ($J_{Al-H}$ = 175 Hz). This SAH solution was analyzed for sodium by acid titration corrected for aluminum hydroxide,[13] for aluminum by precipitation with 8-hydroxyquinoline,[6] and hydride by measuring the hydrogen evolved upon hydrolysis. This solution of SAH in THF was maintained under dry nitrogen in the cold room and analyzed for the hydride concentration periodically to indicate that the solution remained constant at 0.45 M over 2 months at 0 °C.

**General Procedure for Determination of Rate and Stoichiometry.** To a 50-mL flask fitted with a side arm and capped by a rubber septum connected to a gas meter was added 11.1 mL of a 0.45 M solution of SAH in THF (20 mmol in hydride). The flask was immersed in an ice–water bath. The reaction mixture was diluted with 8.9 mL of THF containing 5 mmol of the compound to be reduced. This makes the mixture 0.25 M in the reagent (1.00 M in hydride) and 0.25 M in the compound under investigation. At different time intervals, 4.0-mL sample aliquots were withdrawn and quenched in a THF–0.1 $N$ $H_2SO_4$ hydrolyzing mixture. The hydrogen evolved was measured volumetrically. The reaction was stopped when two or more analyses indicated that no more hydride was taken up. The hydrogen evolved during the reaction was measured volumetrically by an attached gas meter.

The reaction of caproaldehyde is described to examplify the reduction procedure. A 50-mL, oven-dried, round-bottom flask, equipped with a side arm and reflux condenser connected to a gas meter, was placed in an ice–water bath and cooled under dry nitrogen. To this flask were added 11.1 mL of a 0.45 M SAH solution and 3.9 mL of THF. Five mL of a 1.0 M solution of caproaldehyde (5.0 mmol) in THF was injected into the reagent solution rapidly. This made the mixture 1 M in hydride and 0.25 M in the compound. Upon addition of the compound, 1.5 mL of hydrogen evolved, corresponding to 0.01 mmol/mmol of compound. No more hydrogen evolution was observed throughout the reaction. After 5 min, a 4.0-mL aliquot of the reaction mixture was withdrawn and hydrolyzed to indicate 2.98 mmol of residual hydride, which means that 1.01 mmol of hydride per mmol of caproaldehyde had been consumed. After 15 min, an aliquot was also analyzed to indicate the same value of residual hydride, which indicated that the reaction was completed within 5 min. These results are summarized in Table I.

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**Supplementary Material Available:** Ten tables giving the rate and stoichiometry data (14 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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

(12) The solubility of SAH in THF is 3.0 M at 25 °C and 2.9 M at 0 °C.

(13) Furman, N. H. *Standard Methods of Chemical Analysis*; D. Van Nostrand: Princeton, NJ, 1966; Vol. I, p 50.