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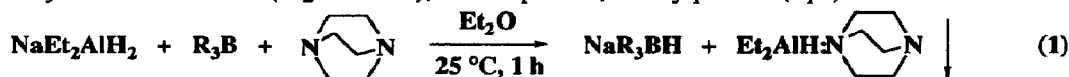
## Lithium Aluminum Hydride-*N*-Methylpyrrolidine Complex. 1. Synthesis and Reactivity of Lithium Aluminum Hydride-*N*-Methylpyrrolidine Complex. An Air and Thermally Stable Reducing Agent Derived from Lithium Aluminum Hydride

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**Summary:** A 1:1 lithium aluminum hydride-*N*-methylpyrrolidine complex (LAHNMP), obtained by the reaction of lithium aluminum hydride with *N*-methylpyrrolidine, is a powerful reducing agent, comparable to lithium aluminum hydride in its reducing properties. LAHNMP reduces esters, lactones, anhydrides and carboxylic acids to the corresponding alcohols. Test reductions show that LAHNMP also reduces a wide range of functional groups, including amides, epoxides, oximes, nitriles, nitro compounds and halides. LAHNMP can be safely transferred in air with the use of a plastic spatula and used in an open container without the need for an inert atmosphere, provided that hydrogen is not evolved during the reduction.

Recently, we investigated the reaction of sodium diethylaluminum hydride (OMH-1) with trialkylboranes in the presence of triethylenediamine (TED).<sup>2</sup> In the course of this work, we obtained diethylaluminum hydride: triethylenediamine adduct (Et<sub>2</sub>AlH:TED), a white powder, as a by-product (eq 1).

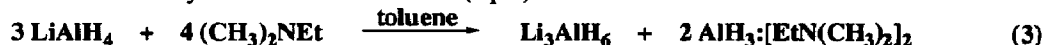


In contrast to the uncomplexed liquid Et<sub>2</sub>AlH, the Et<sub>2</sub>AlH:TED complex can be transferred in open air, and lacks the extreme pyrophoric nature of Et<sub>2</sub>AlH. We were intrigued by the unexpected air stability of Et<sub>2</sub>AlH:TED complex and began to pursue alternate compounds that might be made more directly. Consequently, we were interested in the reaction of various tertiary amines with lithium aluminum hydride (LAH), to check the possibility of forming an air stable LAH:tertiary amine complex.

Dilts and Ashby have reported earlier that treatment of trimethylamine with LAH in benzene produced bis(trimethylamine)-alane and trilithium aluminum hexahydride (eq. 2).<sup>3</sup>



Recently, Marlett and Park<sup>4</sup> reported similar results for the reaction of LAH and dimethylethylamine in toluene as a route to effectively extract alane from LAH (eq. 3).

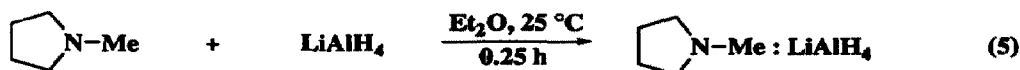


However, the reaction of triethylamine with LAH in benzene yielded a pyrophoric, soluble LAH-triethylamine adduct (eq. 4).<sup>5</sup>



Apparently, the extraction of alane from LAH with tertiary amines is dependent on the nature of the amine and solvent.<sup>6</sup> Initially, we found that the reaction of triethylamine with LAH in Et<sub>2</sub>O yielded LAH-triethylamine adduct as a white solid. However, this complex was extremely pyrophoric when exposed to air.

Fortunately, *N*-methylpyrrolidine reacted with LAH, to give an air stable LAH-*N*-methylpyrrolidine complex (eq. 5).<sup>7</sup>



Herein we report our results on the preparation and characterization of air stable lithium aluminum hydride-*N*-methylpyrrolidine (LAHNMP) complex.<sup>8</sup> LAHNMP is air stable and can be stored in a closed container under dry nitrogen at 25 °C for at least a year without undergoing any decomposition or loss of hydride activity. LAHNMP is not pyrophoric and does not react violently with air. For long-term storage LAHNMP should be kept under nitrogen as the reagent will slowly react with atmospheric oxygen and moisture.

LAHNMP was synthesized by the following procedure: an oven dried, 500-mL round bottom flask equipped with a magnetic stirring bar and rubber septa was charged with 300 mL of a 1 M LAH solution in Et<sub>2</sub>O and 31.2 mL of *N*-methylpyrrolidine (25.5 g, 300 mmol) was added to it with stirring. The reaction was allowed to stir for 0.25 h at 25 °C. During this time a small amount of white solid precipitated from the reaction mixture. The stirring was stopped and the supernatant solution was transferred by double-ended needle to another, oven dried, 500-mL round bottom flask equipped with a magnetic stirring bar and rubber septa. The solvent was evaporated slowly under reduced pressure (10 Torr) to yield LAHNMP as a white powder (32.5 g, 88 %, m. p. 220 °C (decomposition), <sup>27</sup>Al NMR δ 102.5 (q, J = 166 Hz).

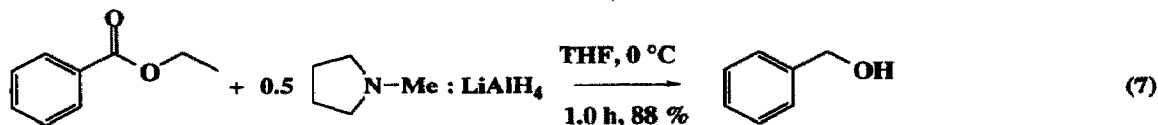
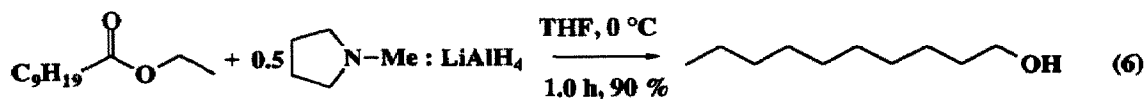
We then carried out isolation-scale reductions on selected compounds containing representative functional groups with LAHNMP in tetrahydrofuran (THF). There is no need to take any special precautions to exclude air and the reductions were performed in open vessels.<sup>9</sup> It was found that LAHNMP was essentially identical to LAH in its reducing power. As shown in Table 1, a wide variety of functional groups were readily reduced.

Table 1. Functional Groups Reduced With LAHNMP<sup>a</sup>

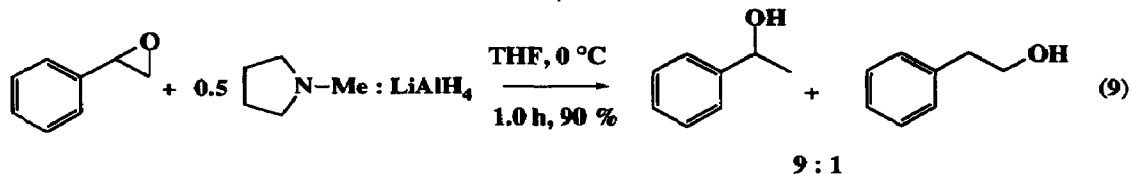
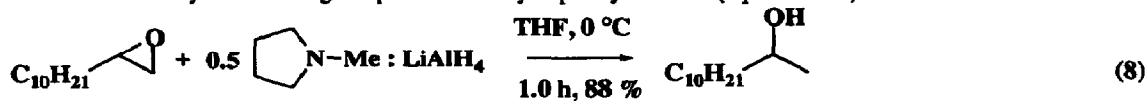
Aldehydes	+	Acids	+	Epoxides	+
Ketones	+	Acid Chlorides	+	Oximes	+
Esters	+	Anhydrides	+	Nitriles	+
Lactones	+	Amides	+	Halides	+
				Nitro	+

<sup>a</sup>See equations for the stoichiometry of the reactants (hydride/compound).

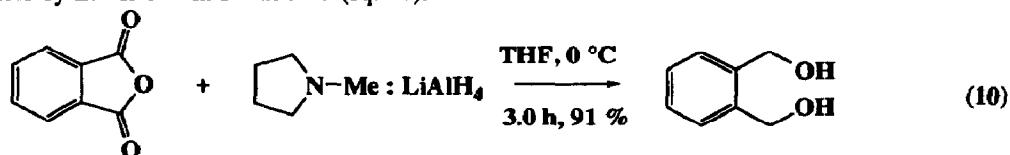
The products from these reduction reactions were easily isolated in high yield and purity. Ethyl decanoate and ethyl benzoate were reduced to the corresponding alcohols in 1.0 h at 0 °C in high yield (eqs. 6 and 7).



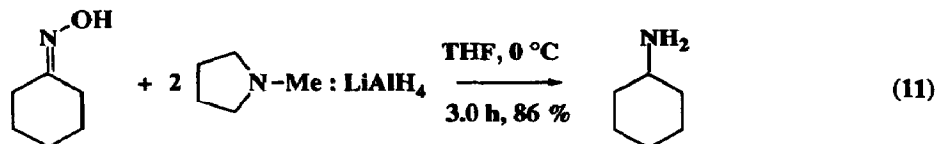
Benzoic acid and acetophenone were reduced to the corresponding alcohols in high yield in 0.5 h at 0 °C. 2-Methylcyclohexanone was reduced to a 88:12 mixture of diastereomers, predominating in the thermodynamically more stable *trans*-2-methylcyclohexanol. 1,2-Epoxydodecane was reduced regioselectively to 2-dodecanol and styrene oxide gave predominantly 1-phenylethanol (eqs. 8 and 9).<sup>10</sup>



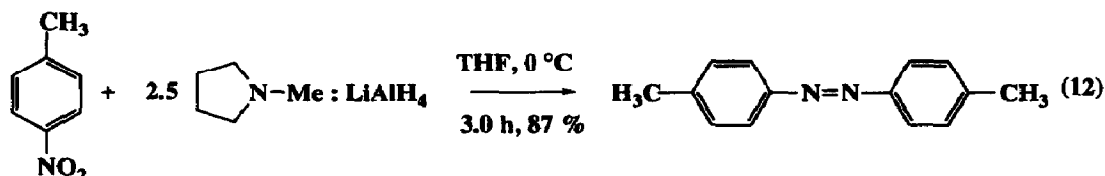
Amides were reduced readily with LAHNMP in 3 h at 0 °C. Thus, benzamide was reduced to benzylamine. *N*-methyldodecanamide was reduced to *N*-methyldodecylamine and *N,N*-diethyldodecanamide was reduced to *N,N*-diethyldodecylamine. Anhydrides, such as phthalic anhydride, were also reduced to the corresponding diols by LAHNMP in 3 h at 0 °C (eq. 10).



Cyclohexanone oxime was reduced with great ease to cyclohexylamine by LAHNMP in 3 h at 0 °C (eq. 11).



Nitriles were reduced by LAHNMP in 3 h at 0 °C. Reduction of benzonitrile gave benzylamine and 3,7-dimethyl-2,6-octadienenitrile was reduced to 2,7-dimethyl-6-octenylamine. Nitro compounds were reduced by LAHNMP as well. In the case of 4-nitrotoluene, reduction with LAHNMP yielded azotoluene in high yield (eq. 12).



Halides were reduced with LAHNMP in 12 h at 25 °C. 1-Bromooctane was reduced to octane and 1-iododecane was reduced to decane. Additionally, benzyl chloride and benzyl bromide were both reduced quantitatively to toluene (eq. 13).<sup>11</sup>



The results summarized in Table 1 indicate that all of the functional groups studied were reduced and LAHNMP is an improvement over LAH in that it can be used without the need to rigorously exclude air in the reduction reaction, provided that hydrogen is not evolved during the reduction. The air and thermal stability makes LAHNMP an excellent reducing agent for large scale reactions.

We are actively exploring the use of other LAH:tertiary amine complexes, including optically active tertiary amines, in the regioselective and stereoselective reduction of organic compounds.

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#### References and Notes

- (1) Complex Chemicals, Corp. 17026 S. E. 40th Place, Bellevue, WA 98008.
- (2) Hubbard, J. L.; Fuller, J. C.; Jackson, T. C.; Singaram, B. *Tetrahedron* **1993**, *49*, 8311.
- (3) Dilts, J. A.; Ashby, E. C. *Inorg. Chem.* **1970**, *9*, 855.
- (4) Marlett, E. M.; Park, W. S. *J. Org. Chem.* **1990**, *55*, 2968.
- (5) Ehrlich, R.; Rice, G. *Inorg. Chem.* **1966**, *5*, 1284.
- (6) Cha, J. C.; Brown, H. C. *J. Org. Chem.* **1993**, *58*, 3974.
- (7) LAHNMP powder was obtained as a gift from Complex Chemicals.
- (8) The white LAHNMP complex was used directly for reductions described in this communication. As a safety precaution, the LAHNMP when not in use should be stored in a closed container free from moisture under nitrogen to avoid any loss of hydride activity over extended periods of time. The transfer of LAHNMP powder from a storage container to a reaction vessel should be done with a plastic spatula.
- (9) The following procedure is representative. An oven dried, 100-mL round bottom flask with stir bar was charged with 2.3 mL of ethyl decanoate (2.00 g, 10 mmol) and 10 mL of THF. LAHNMP (0.75g, 6 mmol) was then added slowly at 0 °C with vigorous stirring. The reaction flask was lightly covered with a septum, to prevent any condensation, and the reaction mixture was allowed to stir for 1.0 h at 0 °C. It was then quenched by sequential addition of 2 mL of H<sub>2</sub>O and 10 mL of HCl (3 M, 30 mmol)[*Caution: Hydrogen evolution*]. The reaction mixture was extracted with Et<sub>2</sub>O (50 mL) and the organic phase was washed with H<sub>2</sub>O (3 X 10 mL) and dried over MgSO<sub>4</sub>. Evaporation of the solvent and distillation of the residue under reduced pressure afforded pure 1-decanol: (1.42 g, 90 %); bp 75 °C (0.16 Torr); IR (neat) 3344, 2926, 1640, 1466, 1378, 1056 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 0.8 (t, *J* = 7 Hz, 2 H), 1.2 (m, 15 H), 1.5 (q, *J* = 8 Hz, 2 H); 2.8 (br s, 1 H), 3.6 (t, *J* = 8 Hz, 2 H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 14.0, 22.7, 25.8, 29.3, 29.4, 29.5, 29.6, 31.9, 32.7, 62.7; *m/z* 158 (M<sup>+</sup>).
- (10) The ratio of alcohol products was determined by 250 MHz <sup>1</sup>H NMR.
- (11) Toluene was identified by capillary GC analysis with internal standards.

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