

**Lithium Aluminum Hydride Reductions; A New Hydrolysis Method for Intractable Products**

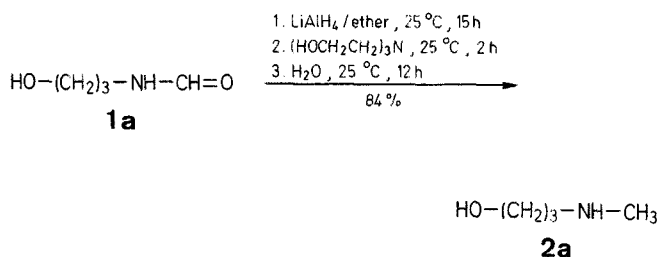
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A new hydrolysis procedure is described for lithium aluminum hydride reductions which allows for simpler technique and markedly improved yields in the synthesis of multifunctional products. The procedure is illustrated by the reduction of a series of formamides and amino-esters to give various propanolamines.

Lithium aluminum hydride reductions play a major role in many organic synthetic procedures. Occasionally difficulties are encountered with regard to the separation of intractable

products when following the usual hydrolysis procedure<sup>1</sup>. For example, difficulties of this type frequently occur when the required organic product can function as a bidentate/multidentate ligand<sup>2-5</sup> and consequently remains strongly bound to the aluminum cations following hydrolysis<sup>6</sup>. One approach to the problems of poor yields associated with product "sticking" to the aluminum residues involves exhaustive Soxhlet extraction using methanol<sup>6</sup>. Although this hydrolysis procedure can be highly efficient based on yields, exhaustive Soxhlet extraction is *cumbersome and limits the scale upon which this approach is applicable*<sup>7</sup>. We herein report a modified hydrolysis method for lithium aluminum hydride reductions which can overcome problems of "intractable products", as illustrated by the synthesis of a series of propanolamines, **2**.



The Table lists a series of amino-compounds **2** (aza-crown ether precursors<sup>7,8</sup>) obtained from lithium aluminum hydride reductions of the appropriate ester or formamide **1**. Using conventional lithium aluminum hydride reduction/hydrolysis procedures<sup>1</sup> followed by prolonged and repeated methanol extractions, which were indeed cumbersome, only very low yields of desired products were obtained (e.g., 10–15% overall yield for **2b** and **2c**). This low yield is *due to the resulting propanolamine 2 being a very good "ligand" for aluminum*. We have found that replacement

of sodium hydroxide/water hydrolysis by triethanolamine (reasonably inexpensive) markedly improves the hydrolysis step both from the aspect of procedure and overall yields.

The improved yields of reduced product using this modified hydrolysis procedure is presumably *due to the triethanolamine being a better "ligand" for aluminum cation than the desired products 2*. It should be noted that these are preliminary results and little effort has been made with a view to maximizing yields by varying reaction conditions or to test the scope of applicability. However, the procedure described should prove useful for synthesis of various multifunctional materials which exhibit strong ligation to aluminum cation.

### 3-Hydroxypropyl-methylamine (**2a**); Typical Procedure:

Formamidine **1a** (64.1 g, 0.62 mol) is slowly added dropwise to lithium aluminum hydride (42.3 g, 1.1 mol) in anhydrous diethyl ether (2000 ml) with stirring by a mechanical stirrer. The addition is completed over a 2.5 h period. The mixture is stirred for an additional 12 h at room temperature. Triethanolamine (160 ml, 1.2 mol) is added to the mixture over a period of 1 h to hydrolyze the lithium aluminum hydride residues. The mixture is stirred an additional hour. Distilled water (40.0 ml, 2.2 mol) is added over a period of 1 h and stirred 12 h during which time the hydrolyzed residues have formed a solid grey/white mass at the bottom of the reaction flask. The solid is broken up to a "sand" consistency using a glass rod, and the ether filtered by gravity through paper. The lithium aluminum hydride residues are then extracted with diethyl ether (6 × 500 ml) and similarly filtered. The ether extractions are combined, solvent removed on a rotary evaporator and the residues vacuum distilled to give **2a**; yield: 46.6 g (84%); b.p. 94–100°C/82 torr (170–175°C corrected to 760 torr).

Several other aza-crown ether precursors were reduced in identical fashion and overall yields after distillation are shown in the table along with observed boiling point data. The new compounds were sent for elemental analysis, also see table. All compounds were characterized by <sup>1</sup>H- and <sup>13</sup>C-N.M.R. spectrometry.

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**Table.** Lithium Aluminum Hydride Reduction of Formamidines or Aminoesters **1**

Substrate <b>1</b>	Product <b>2</b>	Yield [%]	b.p. [°C]/torr	
			found	reported
<b>1a</b> $\text{HO}-(\text{CH}_2)_3-\text{NH}-\text{CH}=\text{O}$	<b>2a</b> $\text{HO}-(\text{CH}_2)_3-\text{NH}-\text{CH}_3$	84	170–175°/atmos.	167–168°/atmos. <sup>9</sup>
<b>1b</b> $\text{HO}-(\text{CH}_2)_2-\text{N}(\text{CH}_3)-(\text{CH}_2)_2-\text{COOC}_2\text{H}_5$	<b>2b</b> $\text{HO}-(\text{CH}_2)_2-\text{N}(\text{CH}_3)-(\text{CH}_2)_2-\text{OH}$	51	315–330°/atmos.	280–330°/atmos. <sup>10</sup>
<b>1c</b> $\text{H}_3\text{C}-\text{N}(\text{CH}_2)_2-\text{COOC}_2\text{H}_5$	<b>2c</b> $\text{H}_3\text{C}-\text{N}(\text{CH}_2)_2-\text{OH}$	68	300–325°/atmos.	290–320°/atmos. <sup>11</sup>
<b>1d</b> $i\text{-C}_3\text{H}_7-\text{N}(\text{CH}_2)_2-\text{COOC}_2\text{H}_5$	<b>2d</b> $i\text{-C}_3\text{H}_7-\text{N}(\text{CH}_2)_2-\text{OH}$	75	295–315°/atmos.	295°/atmos. <sup>12</sup>
<b>1e</b> $i\text{-C}_3\text{H}_7-\text{N}(\text{CH}_2)_2-\text{COOC}_2\text{H}_5$	<b>2e</b> $i\text{-C}_3\text{H}_7-\text{N}(\text{CH}_2)_3-\text{OH}$	83	305–320°/atmos.	305°/atmos. <sup>11</sup>
<b>1f</b> $\text{C}_6\text{H}_{10}\text{N}(\text{CH}_2)_2-\text{COOC}_2\text{H}_5$	<b>2f</b> $\text{C}_6\text{H}_{10}\text{N}(\text{CH}_2)_2-\text{OH}$	77	155–160°/0.5	— <sup>a</sup>
<b>1g</b> $\text{HO}-\text{CH}_2-\text{C}_6\text{H}_{10}\text{N}(\text{CH}_2)_2-\text{COOC}_2\text{H}_5$	<b>2g</b> $\text{HO}-\text{CH}_2-\text{C}_6\text{H}_{10}\text{N}(\text{CH}_2)_3-\text{OH}$	66	145–150°/0.5	— <sup>b</sup>

<sup>a</sup>  $\text{C}_{10}\text{H}_{21}\text{NO}_2$  (187.3) calc. C 64.13 H 11.30 N 7.48  
found 63.30 11.29 7.33

<sup>b</sup>  $\text{C}_9\text{H}_{19}\text{NO}_2$  (173.3) calc. C 62.39 H 11.05 N 8.09  
found 68.83 10.98 8.08

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