# Modified Sodium Bis[2-methoxyethoxy]aluminum Hydride Reagents for the Partial Reduction of Lactones and Esters

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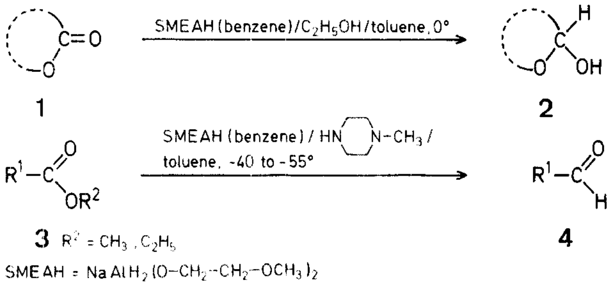
It is known that the reducing power of lithium aluminum hydride (lithium alanate), sodium aluminumhydride, and aluminum hydride is modified by the introduction of alkoxy or amino substituents, and these alkoxy- or aminoaluminumhydrides find routine application for the selective, partial, and stereospecific reductions of various carbonyl and other functionalities[1]. In this communication we report the results obtained with two modifications of the sodium bis[2-methoxyethoxy]aluminumhydride (SMEAH) solution[2,3] which are useful for the partial reduction of lactones to lactols and of esters to aldehydes respectively.

The first reagent (Type I) is simply prepared by the addition of one equivalent of absolute ethanol to the SMEAH solution; it smoothly reduces lactones to lactols. The γ-lactones **1a, b, c** were reduced selectively at 0° to afford the corresponding lactols **2a, b, c** in good yields. In the case of the δ-lactone **1d** (dihydrocoumarin), lower temperature was necessary in order to obtain the desired partial reduction. When the SMEAH reagent without the above treatment was used, the reaction proceeded uncontrolled and gave the lactols only in poor yields.

The first reagent is still not sufficient for the partial reduction of esters (**3**) to aldehydes (**4**). Recently, Muraki and Mukaiyama[4,5] reported that carboxylic acids and esters are converted to the corresponding aldehydes in good yields by reduction with diaminoaluminum hydrides such as bis[4-methyl-1-piperazino]aluminum hydride and dimorpholinoaluminum hydride. We have found that the addition of one equivalent of *N*-methylpiperazine or morpholine to the SMEAH solutions affords an excellent reagent (Type II) for the partial reduction of carboxylic esters (**3**) to aldehydes (**4**) which gives even better yields than diaminoaluminum hydrides.



### Reduction of Lactone 1c with SMEAH Solution Type I:

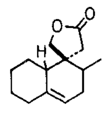
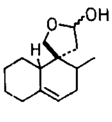
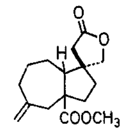
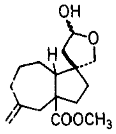
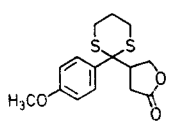
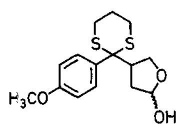
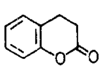
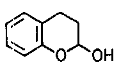
*Modified SMEAH Solution Type I:* A solution of sodium bis[2-methoxyethoxy]aluminum hydride ("SMEAH solution"; 50% in benzene; 2 ml, 5.1 mmol) and toluene (2 ml) are placed in a pear-shaped 30-ml flask stoppered with a serum cap and kept under a nitrogen atmosphere. This solution is stirred at 0°, and a mixture of ethanol (0.3 ml, 5.1 mmol) and toluene (1.7 ml) is added dropwise by means of a syringe. The SMEAH solution Type I is then ready for use.

*Reduction of Lactone* **1c**: The reduction is carried under a nitrogen atmosphere with strict exclusion of moisture. The SMEAH solution (1.2 ml) is added, dropwise and with stirring, to a solution of lactone **1c** (150 mg, 0.49 mmol) in toluene. After 25 min, the reaction is quenched by the addition of water. The mixture is acidified with dilute hydrochloric acid and extracted with benzene. The benzene extract is dried and evaporated and the crude product purified by preparative T.L.C. to give the lactol **2c** as a colorless viscous oil; yield: 126 mg (84%).

### Reduction of Methyl 3-(4-Methoxyphenyl)propanoate (3a) with SMEAH Solution Type II:

*Modified SMEAH Solution Type II:* A solution of sodium bis[2-methoxyethoxyaluminum hydride ("SMEAH solution"; 53% in benzene; 2 ml, 5.5 mmol) and toluene (2 ml) are placed in a pear-shaped 30-ml flask stoppered with a serum cap and kept under a nitrogen atmosphere. This solution is stirred at 0°, and a mixture of 1-methylhexahydropyrazine (*N*-methylpiperazine; 0.65 ml, 6.05

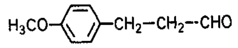
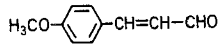
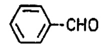
**Table 1.** Reduction of Lactones (**1**) to Lactols (**2**) with SMEAH Solution Type I

| | 1 | | 2 | Reaction conditions | Yield[a] [%] | m.p. | (m.p. Lit.) |
|---|---|---|---|---|---|---|---|
| **a** |  | → |  | 0°, 60 min | 94 | 141–143[6] | |
| **b** |  | → |  | 0°, 45 min | 83 | oil[6] | — |
| **c** |  | → |  | 0°, 25 min | 84 | oil | — |
| **d** |  | → |  | −70°, 80 min<br>−60°, 15 min<br>0°, 30 min | 63<br>64[b]<br>43 | oil | 28°[7] |

[a] Yield of isolated pure product.

[b] As 2,4-dinitrophenylhydrazone of the corresponding 3-(2-hydroxyphenyl)-propanal; m.p. 183–185° (Lit.[7] 185°).

**Table 2.** Reduction of Alkyl Carboxylates (**3**) to Aldehydes (**4**) with SMEAH Solution Type II

| | Aldehyde **4** | Reaction conditions | Yield[c] [%] | m.p. | (m.p. Lit.) |
|---|---|---|---|---|---|
| **a** |  | −55° to −40°, 70 min[a] | 88 | oil | — |
| | | 0°, 35 min[a] | 54 | | |
| | | 0°, 45 min[b] | 49 | | |
| **b** |  | 0°, 30 min[b] | 84 | [259–260°][d] | [268–270°][8] |
| | | 0°, 13 min[a] | 70 | | |
| **c** |  | −10°, 35 min[a] | 85[d] | 231–232° | 233–234°[9] |

[a] Reagent prepared with *N*-methylpiperazine.

[b] Reagent prepared with morpholine.

[c] Yield of isolated pure product.

[d] As 2,4-dinitrophenylhydrazone.

mmol) [or morpholine (0.53 g, 6.08 mmol)] and toluene (3 ml) is added dropwise by means of a syringe. The SMEAH solution Type II is then ready for use.

*Reduction of 3-(4-Methylphenyl)-propanoate* (**3a**): The reduction is carried out under a nitrogen atmosphere with strict exclusion of moisture. The SMEAH solution (4.6 ml) is added, dropwise and with stirring, to a solution of the ester **3a** (115 mg, 0.59 mmol) in toluene (6 ml) at −40°. Stirring is continued for 70 min at −40° to −55°. Then, the reaction is quenched by the addition of water. The mixture is acidified and extracted with benzene. The organic extract is dried and evaporated and the crude product purified by column chromatography on silica gel (benzene as eluent) to give *3-(4-methylphenyl)-propanal* (**4a**) as an oil; yield: 86 mg (88%).

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[2] SMEAH solution is commercially available.

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