Lithium Aluminium Hydride Reduction in Non-Polar Solvents: Use of Silica Gel as an Effective Catalyst

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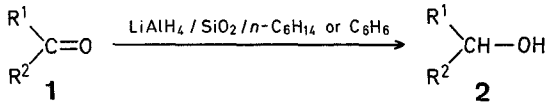
In recent years silica gel has been used as an effective catalyst to control the intrinsic activity of reagents[1]. For example, with the use of conventional reagents, highly selective reactions could be realized in the presence of silica gel[2,3,4]. In other cases, a small amount of added silica gel changed the nature of the reagents completely and new reactions could be observed[2,5-8]. Silica gel can also be used as a mild and therefore very selective Lewis acid catalyst[9].

Lithium aluminium hydride has long been known as a reagent for the reduction of carbonyl compounds and esters to alcohols and is now widely used. However, its use is sometimes seriously limited by solubility problems; diethyl ether, tetrahydrofuran and some alternative polyethers are conventional solvents but hydrocarbons such as *n*-hexane and benzene cannot be used for this purpose. We have found that lithium aluminium hydride on silica gel is a good reagent for the reduction in non-polar solvents.



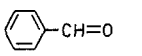
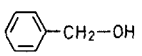
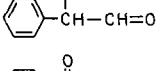
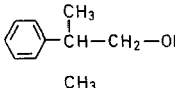
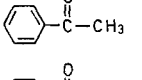
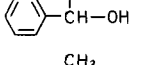
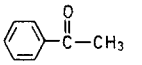
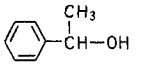
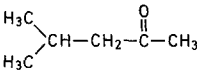
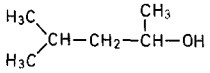
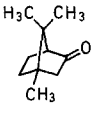
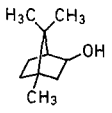
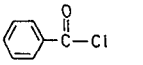
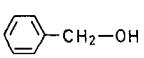
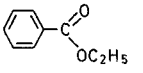
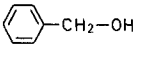
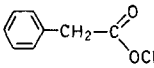
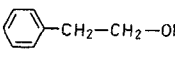
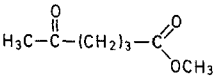
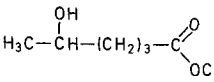
1 **2**

The reactions proceed quite cleanly at room temperature and no detectable amount of starting material or by-products can be detected even by careful inspection of the crude products by ^{1}H-N.M.R. Aliphatic as well as aromatic aldehydes, ketones, and acid chlorides **1a–f** were all converted into the corresponding alcohols **2a–f** in fair yields. The reduction of esters (e.g. **1g, i**) proceeds more slowly and requires higher temperatures (e.g. boiling *n*-hexane). The difference in reactivity between ketones and esters enables the selective reduction of keto esters into hydroxy esters by the reagent in non-polar solvents. This is demonstrated by the reduction of methyl 4-acetylbutanoate **(1i)** to methyl 5-hydroxyhexanoate **(2i)** by the reagent in *n*-hexane at room temperature.

Recently, sodium borohydride on neutral alumina was reported to be a reducing reagent usable in non-polar solvents[10,11,12]. However, this reagent cannot be used for the reduction of esters. Furthermore, camphor **(1e)**, readily reduced to isoborneol **(2e)** by our reagent, is reported to react sluggishly with the former reagent[11].

Lithium Aluminium Hydride - Silica Gel Reagent:
Commercial grade silica gel (Waco gel C-300, for column chromatography) is dried at 150–170 °C for 3 h under reduced pressure (~5 torr). To a mixture of dried silica gel (1.0 g) and lithium aluminium hydride (0.114 g, 3 mmol) dry diethyl ether (5 ml) is added. After stirring for 2 h the reaction mixture is evaporated to dryness under reduced pressure to afford the reagent as a slightly grayish powder which should be used directly for the reduction without removal from the reaction vessel. When stored in a desiccator the reagent slowly decomposes.

Table. Reductions with Lithium Aluminium Hydride on Silica Gel in Non-Polar Solvents (3 h at 25 °C)

Substrate	Product[a] **2**	Amounts used 1 (mmol)/$LiAlH_4$ (mmol)/SiO_2 (g)	Solvent (ml)	Yield [%]	m.p. [°C] or b.p. [°C]/torr found	reported
1a 		1.0/3.0/1.0	*n*-hexane (10)	~100	205°/760	205°/760[14]
1b 		1.0/3.0/1.0	*n*-hexane (10)	81	110–111°/10	105–106°/11[15]
1c 		0.5/1.5/0.5	*n*-hexane (5)	82	204°/745	203°/760[14]
1c 		0.5/1.5/0.5	benzene (5)	85		
1d 		1.0/3.0/1.0	*n*-hexane (10)	74	130°/734	133°/760[14]
1e 		2.0/6.0/2.0	*n*-hexane (10)	69	212°	212–214°[14]
1f 		1.0/6.0/2.0	*n*-hexane (10)	~100		
1g 		1.0/6.0/2.0[b]	*n*-hexane (10)	83		
1h 		1.0/6.0/2.0[b]	*n*-hexane (10)	~100	219–221°/750	218°/760[14]
1i 		1.0/3.0/1.0	*n*-hexane (10)	62	44°/0.01	44°/0.01[13]

[a] ^{1}H-N.M.R. and I.R. spectra are in accord with those of authentic samples.
[b] Reaction at reflux temperature for 3 h.

Reduction of Benzaldehyde; Typical Procedure:
To the freshly prepared reagent, dry *n*-hexane (10 ml) and then benzaldehyde (106 mg, 1.0 mmol) are added under an atmosphere of nitrogen. After stirring for 3 h at 25 °C (at the reflux temperature in the cases of esters), the excess reagent is quenched with a saturated aqueous solution of ammonium chloride (0.3 ml); the mixture is filtered and the silica gel washed thoroughly with diethyl ether (10 ml). The filtrate and the washings are combined and the solvent is removed to give benzyl alcohol; yield: 110 mg (~ 100%). Without further purification, the product is found to be essentially pure by ^{1}H-N.M.R.

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