

SELECTIVE REDUCTIONS WITH ALUMINUM HYDRIDE

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IN contrast to the reducing action of lithium aluminum hydride, which has been widely studied, the reducing properties of aluminum hydride² have been of very little concern. It is generally believed that the function of aluminum hydride as a reducing agent is similar to that of lithium aluminum hydride,³ from which it can be prepared by the following stoichiometry:⁴



We now wish to report a class of reactions in which aluminum hydride differs from lithium aluminum hydride. Reductions of multiple bonds when these are in conjugation with an aromatic ring and a reducible functional group by lithium aluminum hydride have been observed.⁵ We have shown that

- ¹ The author gratefully acknowledges a postdoctoral fellowship from the Division of General Medical Sciences, U.S. Public Health Service, 1959-1961.
- ² E. Wiberg, Angew. Chem. **63**, 485 (1951) and subsequent papers by the same author.
- ³ E. Wiberg and A. Jahn, Z. Naturf. **7B**, 580 (1951); E.L. Eliel and M.N. Rerick, J. Amer. Chem. Soc. **82**, 1367 (1960).
- ⁴ When the ratio of aluminum chloride to lithium aluminum hydride is larger than 1/3, new reducing species AlH_2Cl and/or AlHCl_2 are produced. The reducing action of these "mixed hydrides" has been the subject of excellent reviews: E.L. Eliel, Rec. Chem. Progr. **22**, No. 3 (1961); M.N. Rerick; The Mixed Hydrides. Metal Hydrides, Inc., Beverly, Mass. (1959).
- ⁵ See, for example, ^a R.F. Nystron and W.G. Brown, J. Amer. Chem. Soc. **69**, 2548 (1947); ^b F.A. Hochstein and W.G. Brown, Ibid. **70**, 3484 (1948); ^c F.A. Hochstein, Ibid. **71**, 305 (1949); ^d C.S. Rondestvedt, Jr., Ibid. **73**, 4509 (1951); ^e P. Karrer and P. Banerjee, Helv. Chim. Acta **32**, 1692 (1949); ^f A. Dornow, G. Messwarb and H.H. Frey, Chem. Ber. **83**, 495 (1950); ^g E.B. Bates, E.R.H. Jones and M.C. Whiting, J. Chem. Soc. 1854 (1954).

aluminum hydride can be employed to prevent such reductions. Thus, cinnamaldehyde and ethyl cinnamate were reduced smoothly in excellent yields to cinnamyl alcohol by aluminum hydride;⁶ similarly, methyl phenylpropionate was converted to phenylpropargyl alcohol. Lithium aluminum hydride under similar conditions afforded only the further reduction products hydrocinnamyl alcohol and cinnamyl alcohol, respectively. Although the course of the lithium aluminum hydride reduction can often be directed to prevent multiple bond reduction by the proper choice of reaction conditions,⁷ the necessary control is cumbersome. By contrast, the selectivity of the aluminum hydride method was found to be insensitive to vigorous reaction conditions as well as to the presence of lithium aluminum hydride (cf. Table 1).

More significantly, we have shown that aluminum hydride, in addition to being a more conveniently employed reagent than lithium aluminum hydride, affords a selectivity beyond that obtainable by controlled lithium aluminum hydride reduction. Methyl o-coumarate could not be reduced to o-hydroxycinnamyl alcohol by lithium aluminum hydride even under the most carefully chosen conditions.^{5a,8} Aluminum hydride, on the other hand, afforded a good yield of trans o-hydroxycinnamyl alcohol.⁹ This method, therefore, promises

⁶ In a typical reduction sufficient aluminum chloride to give more than the stoichiometrically required amount of aluminum hydride was added to a cooled solution of lithium aluminum hydride in ether; dissolution of aluminum chloride and precipitation of lithium chloride took place readily upon warming to room temperature. An ethereal solution of the substrate was then added, and the reaction allowed to proceed at room temperature for 30 min. Solutions of aluminum hydride were generally employed as generated in situ, containing both precipitated lithium chloride and some polymeric aluminum hydride; filtered solutions gave identical results.

⁷ The amount of control necessary depends on the rate at which the multiple bond reduction takes place. For cinnamaldehyde, in contrast to previous reports,^{5b} the only control needed is a short reaction time (cf. footnote 11); the reduction of methyl phenylpropionate requires slow inverse addition of the stoichiometric amount of lithium aluminum hydride.

⁸ The reaction product upon chromatographic work-up was found to consist of unreacted ester, o-hydroxyhydrocinnamyl alcohol and methyl o-hydroxyphenylpropionate. The double bond reduction in this case presumably proceeds via the initially formed phenoxy lithium aluminumhydride and is being further investigated.

⁹ Isolated in pure state, m.p. 86-87°, in 75 per cent yield from chromatography on silicic acid; satisfactory analysis was obtained.

to become a general pathway to unsaturated alcohols which are difficult or impossible to prepare by reduction with lithium aluminum hydride on account of preferred or competing double bond reduction through carbon-aluminum bond formation^{5b} (*vide infra*). The applicability of this method to prevention of other reductions of double bonds, proceeding with ease by lithium aluminum hydride,¹⁰ is being explored.

TABLE 1
Reduction of Cinnamaldehyde

Molar proportion ^a		Product ^b	Reaction conditions
LiAlH ₄	AlH ₃		
-	1.8 0.9 2.4	Cinnamyl alcohol	30 min or 5 hr at room temperature
0.65	-	Hydrocinnamyl alcohol	30 min at room temperature
0.4 1.5	0.8 0.6	Cinnamyl alcohol	Hydride mixture used as generated <i>in situ</i> , or clear solution of AlH ₃ added concurrently with or subsequent to LiAlH ₄ . 30 min at room temperature.
0.9	0.20	Mixture of cinnamyl and hydrocinnamyl alcohols	30 min at room temperature

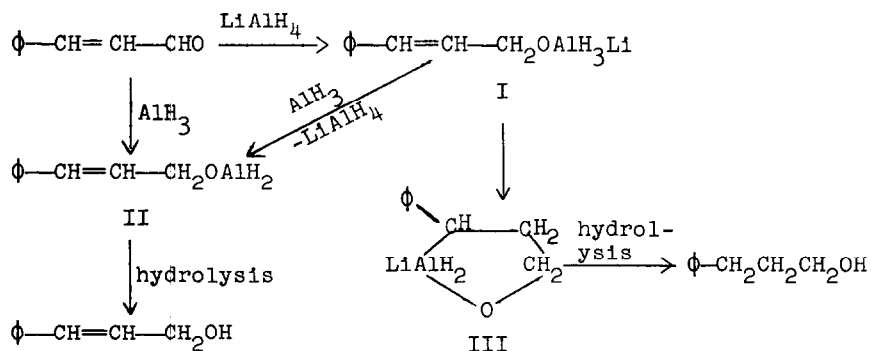
^a Cinnamaldehyde taken as unity.

^b Product composition generally obtained from infrared analysis and m.p. of product (cinnamyl alcohol m.p. 33°, hydrocinnamyl alcohol m.p. below -18°). Vapor phase chromatography indicated that small amounts (<10 per cent total) of other product, possibly 1-phenyl-2-propene-1-ol and 1-phenylpropanol were also formed. Yields were in the order of 90 per cent on a 10 mmole scale.

The presence of large amounts of lithium aluminum hydride in solution (*cf.* Table 1) did not change the course of the aluminum hydride reduction. Even when a large quantity of lithium aluminum hydride was added *first* to

¹⁰ See, for example, J.S. Meek and R.D. Stacy, *J. Org. Chem.* **26**, 300 (1961); P.R. Story, *Ibid.* **26**, 287 (1961); M.R. Mousseron *et al.*, *Bull. Soc. Chim. Fr.* [5], **19**, 1042 (1952); *C.R. Acad. Sci., Paris* **235**, 177 (1952).

the substrate (cinnamaldehyde), to give a fast reduction of the carbonyl,¹¹ followed by the addition of a solution of excess aluminum hydride, no double bond reduction was observed. These exploratory studies suggest that unlike I, the alkoxyaluminumhydride II, if present, is incapable of undergoing the subsequent reduction (I to III) postulated for I.^{5b} Furthermore, it appears that in the presence of aluminum hydride I undergoes an exchange reaction to give II, accounting for the maintained selectivity in the presence of lithium aluminum hydride. The mechanistic aspects of this sequence of reactions is being further investigated.



¹¹ Work-up of the solution at this stage (about 2 min) gave pure cinnamyl alcohol, but when allowed to react for 30 min, the same mode of addition gave only hydrocinnamyl alcohol.