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LITHIUM ALUMINUM HYDRIDE ON SILICA GEL - SELECTIVE REDUCTION OF KETONES AND CARBOXY ESTERS IN THE PRESENCE OF NITRO AND CYANO GROUPS

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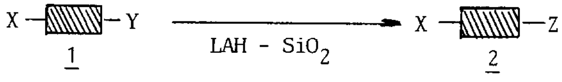
Abstract: Cyano and nitro groups were found not to be reduced by lithium aluminum hydride on silica gel and with the use of this reagent ketones and carboxy esters bearing cyano and nitro groups were successfully converted into the corresponding cyano and nitro alcohols.

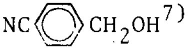
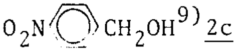
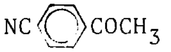
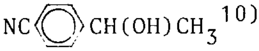
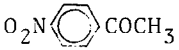
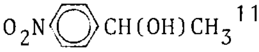
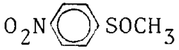
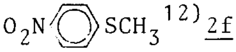
Although lithium aluminum hydride (LAH) has long been used as a versatile reagent for reducing carbonyl compounds and carboxy esters into alcohols, its selectivity is not sufficient to discriminate these two types of compounds. Nitro and cyano groups and so on1) are also known to be reduced by LAH in ordinary conditions.2) Recently we reported that when LAH is used in the presence of silica gel (LAH-SiO_2) the reduction can be carried out in n-hexane or in benzene as solvent3) and that the selectivity of LAH is strongly enhanced to result in successful reduction of ketoesters to the corresponding hydroxyesters.4)

We now wish to communicate here that LAH-SiO_2 in anhydrous diethyl ether can reduce carboxy esters as well as ketones bearing cyano and nitro groups into the corresponding cyano and nitro alcohols in fair yields. The reaction proceeds quite cleanly under usual reaction conditions and the raw products were found to be practically pure by ^{1}H-NMR spectra. Results for selective reduction of some representative cyano and nitro esters and ketones by LAH-SiO_2 are summarized in Table 1. Typical procedure for this reaction is as follows. To a mixture of silica gel5) (1.4 g) and LAH (4 mmol) was added 5 ml of dry diethyl ether under atmosphere of nitrogen. After the whole mixture had been stirred for 1 h 1 mmol of methyl p-cyanobenzoate was added and then refluxed for 3 h. After the mixture had been cooled and quenched with a few drops of saturated aqueous solution of NH_4Cl, the silica gel was filtered off and washed thoroughly with diethyl ether. The filtrate and the washings were combined and evaporated in vacuo to give 77 % yield of p-cyanobenzyl alcohol. Reaction time and temperature are not critical in this reaction. In addition, amounts of LAH-SiO_2 are not so critical, too. For instance, use of increased amounts of LAH(1.5 times) and SiO_2(1.5 times) compared to the case of the typical procedure described above did not affect the yield of p-cyanobenzyl alcohol and any indications showing



X= NO_2, CN Y= CO_2R, COR, SOR
Z= CH_2OH, CH(OH)R, SR

Table 1. Results of Selective Reduction with the Use of LAH-SiO_2.

Substrate(1 mmol)		LAH(mmol)	SiO_2(g)	Temp.(°C)	Time(h)	Product[6]		
	1a	4.0	1.3	refl.	3	 [7]	2a	67%
	1a	6.0	2.0	refl.	3		2a	73%
$NCCH_2CO_2CH_3$	1b	3.0	1.0	refl.	3	$NCCH_2CH_2OH$[8]	2b	54%
	1c	3.3	1.0	20	3	 [9]	2c	66%
	1d	1.4	0.7	20	2	 [10]	2d	77%
	1e	1.4	0.7	20	2	 [11]	2e	82%
	1f	2.8	1.4	20	2	 [12]	2f	73%

* For all experiments 5 ml of dry diethyl ether was used as a solvent.

reduction of the cyano group were not observed even by careful inspection of the raw products by ^1H-NMR. Similarly methyl cyanoacetate, methyl p-nitrobenzoate, p-cyanoacetophenone and p-nitroacetophenone were successfully converted to the corresponding cyano and nitro alcohols. This reagent also selectively reduced sulfinyl group of methyl p-nitrophenyl sulfoxide and afforded methyl p-nitro sulfide in fair yield.

References and Notes

1) "Organic Reactions", VI, p 496, John Wiley & Sons, Inc. New York.

2) It was reported that nitro and cyano groups were not reduced by LAH under carefully controlled conditions involving lower temperatures, inverse additions and high dilution method. (I. E. Felkin, H. Felkin, Z. Wervart, *Compt. Rend.*, 234, 1789 (1952); C. F. Huebner, C. R. Scholz, *J. Am. Chem. Soc.*, 73, 2089 (1951); A. W. D. Avison and A. L. Morrison, *J. Chem. Soc.*, 1474 (1950).

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5) Commercial grade silica gel (Wakogel C 300) dried at 150 - 170°C for 3 h in vacuo was used for all experiments.

6) ^1H- NMR (60 MHz, δ in $CDCl_3$): 2a, 7.16 - 7.65 (q, 4H), 4.63 (s, 2H), 3.50 (br, 1H); 2b, 3.73 (t, 2H), 3.53 (br, 1H), 2.51 (t, 2H); 2c, 7.40 - 8.33 (q, 4H), 4.82 (s, 2H), 2.03 (br, 1H); 2d, 7.30 - 7.73 (q, 4H), 4.89 (q, 1H), 2.70 (br, 1H), 1.43 (d, 3H); 2e, 7.33 - 8.27 (q, 4H), 4.97 (q, 1H), 2.58 (br, 1H), 1.50 (d, 3H); 2f, 7.19 - 8.23 (q, 4H), 2.53 ppm (s, 3H).

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