Copper(I)-catalysed Conjugate Reduction of αβ-Unsaturated Carbonyl Compounds by Lithium Aluminium Hydride

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Summary CuI catalyses an efficient conjugate reduction of αβ-unsaturated carbonyl compounds by $LiAlH_4$ in the presence of hexamethylphosphoric triamide at −78 °C.

CONJUGATE reduction of αβ-unsaturated carbonyl compounds by means of complex copper hydrides,[1] or the reagents[2] obtained by the combination of complex metal hydrides with a stoicheiometric amount of copper salts, has attracted considerable interest in recent years. However, these reagents are generally required to be used in a large excess over the αβ-unsaturated carbonyl compounds. Moreover, the copper hydride reagents are not readily accessible. Here we report efficient CuI-catalysed conjugate reduction of αβ-unsaturated carbonyl compounds by $LiAlH_4$ (LAH) in the presence of hexamethylphosphoric triamide (HMPA) as a co-solvent.

All operations described here were carried out under nitrogen, and the present CuI-catalysed conjugate reduction of αβ-unsaturated carbonyl compounds by LAH was examined mainly using cyclohexenone. To a suspension of LAH† (*ca.* 1 mmol) in tetrahydrofuran (THF) at −78 °C, was added CuI dissolved in THF–HMPA (1 ml each). The resulting mixture was stirred for 30 min at −78 °C, and then cyclohexenone was added. After stirring for 60 min at −78 °C, the mixture was treated with saturated aqueous NH_4Cl (3 ml) followed by ether (3 ml). The organic layer was directly analysed by g.l.c. The results are summarised in Table 1. The features of the reducton of cyclohexenone by the combination of LAH and CuI are as follows: i, HMPA is essential for effecting the regioselective conjugate reduction, ii, the amount of CuI can be reduced to 1—5 mol% of LAH (thus, CuI functions as a catalyst), and iii, there is no need to use a large excess of LAH over cyclohexenone. The hydride anions of LAH are effectively utilized for the conjugate reduction.

Table 2 summarizes the results of LAH–CuI reductions of other αβ-unsaturated carbonyl compounds. The conjugate reduction of mesityl oxide and benzylideneacetone occurred smoothly by the use of an equimolar mixture of the enones and LAH with 10 mol% CuI. The conjugate reductions of both an αβ-unsaturated aldehyde and a similar ester were also accomplished. *trans*-Hex-2-enal and methyl crotonate

TABLE 1. Reduction of cyclohex-2-enone by the combination of LAH and CuI at −78 °C.[a]

Molar ratio				% Yield of products[b]			
Cyclohexenone: LAH	CuI: LAH	HMPA: THF (v/v)	Time /min	Cyclohexanone	Cyclohex-2-enol	Cyclohexanol	% Unchanged cyclohexenone
1:1	1:1	1:4	60	91	2	3	0
1:1	1:20	1:4	60	85	0	4	0
1:1	1:1	0	60	33	42	3	0
1:1	0	1:4	60	30	trace	20	4
1:1	0	0	60	12	64	15	0
3:1	1:10	1:4	60	88	2	2	0
3:1	1:20	1:4	60	88	2	2	3
3:1	1:100	1:4	60	69	3	2	6
3:1	1:10	1:16[c]	60	86	5	2	0
3:1	1:20	0	60	40	30	1	13
3:1	0	1:4	60	28	8	3	11
3:1	1:10	1:4	10	89	5	1	4
3:1	0	1:4	10	16	1	6	41

[a] LAH; 1·0—1·5 mmol; Solvent; 5—6 ml. [b] Based on starting cyclohexenone. [c] The molar ratio of HMPA to LAH was 1·2:1.

TABLE 2. Reduction of αβ-unsaturated carbonyl compounds by combinations of LAH and CuI.[a]

			Product yield %[b]			
Substrate (S)	S:LAH (molar ratio)	CuI:LAH (molar ratio)	1,4	1,2	1,4 + 1,2	% Unchanged S
Mesityl oxide	1:1	1:10	82	trace	trace	2
	1:1	0	4	3	trace	74
	3:1	1:10	72	4	1	11
Benzylideneacetone	1:1	1:10	91	3	0	0
	1:1	0	5	3	2	55
trans-Hex-2-enal	1:1	1:10	63	12	1	1
	1:1	0	2	52	0	5
Methyl crotonate	1:1	1:10	52	0	trace	0
	1:1	0	0	0	0	98

[a] LAH: 1·0—1·5 mmol; solvent; 5—6 ml of THF–HMPA (4:1, v/v); temp; −78 °C; time; 60 min. [b] Based on αβ-unsaturated carbonyl compound; 1,4-reduction = reduction of double bond; 1,2-reduction = reduction of >C=O to >CHOH.

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† Commercially available LAH from Metallgesellschaft A. G. was used directly.

were satisfactorily reduced at the carbon–carbon double bond, although the conjugate reduction of cinnamaldehyde and methyl cinnamate, containing a phenyl-substituted carbon–carbon double bond, proceeded less effectively Thus, the present study is the first example of the conjugate reduction of $\alpha\beta$-unsaturated carbonyl compounds by the combination of complex metal hydrides with a catalytic amount of copper salts, and provides a convenient method for this type of reaction

The reduction of cyclohexenone to cyclohexanone after only a short reaction time, and the reductions of mesityl oxide and benzylideneacetone, clearly demonstrate that an active species generated from CuI and LAH reduces the carbon–carbon double bond of the substrates much faster than reduction by LAH alone Other copper(I) compounds such as mesitylcopper(I)[3] and copper(I) t-butoxide can be used instead of CuI On the basis of the effective utilization of the hydride anions of LAH and the conjugate reduction by an equimolar mixture of LAH and CuI, together with previous reports of complex copper hydride reagents,[1] the active reducing species may be assumed to be an ate-complex of copper(I) hydride, LiHCuR (R = I, mesityl, or Bu^tO) Mechanistic studies on the active reducing species, the role of aluminium hydride, and the function of HMPA,[1a,4] as well as application of the present reducing system to other functional groups,‡ are now in progress

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‡ We have reduced crotononitrile and phenylacetylene to n butyronitrile and styrene, respectively, by the combination of LAH and CuI

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