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Conjugate Reduction of 2-Butene-1,4-diones with $LiAlH_4$-$SbCl_3$

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(Received June 15, 1990)

Synopsis. The reagent $LiAlH_4$–$SbCl_3$ was found to be more effective for a conjugate reduction of 2-butene-1,4-diones in comparison with the reagent $LiAlH_4$–other metal halides.

The effect of the addition of $AlCl_3$ to $LiAlH_4$ was to produce more mild and specific reagents for reducing epoxides and halo ketones.[1] Therefore, a chemoselective reduction of polyfunctional compounds with $LiAlH_4$ in the presence of various other metal halides has been the subject of much study.[2] It was reported that the reduction of α,β-unsaturated ketones with $LiAlH_4$–Cu_2I_2 or $LiAlH_4$–metal halides (e.g., Cu_2Br_2, Cu_2Cl_2, $TiCl_3$, $FeCl_3$) gave the corresponding ketones arising from a conjugate reduction.[3,4] Since γ-keto-α,β-unsaturated ketones, such as 2-butene-1,4-diones, afforded 1,2-reduction products predominantly with $LiAlH_4$ or $NaBH_4$, there has been much interest in mild, convenient methods for a conjugate reduction of γ-keto-α,β-unsaturated ketones. The reduction of γ-keto-α,β-unsaturated ketones with $LiAlH_4$–metal halides, however, has not been carried out.[1–7] Moreover, $SbCl_3$ has not been used as a metal halide in a conjugate reduction of α,β-unsaturated ketones and γ-keto-α,β-unsaturated ketones. Since antimony is one of the representative elements which possess both metallic and nonmetallic properties and Sb^{3+} is a borderline acid in the classification of hard and soft acids,[2a,6,7] it can be expected that the reduction of carbonyl compounds with $LiAlH_4$–$SbCl_3$ has a new reactivity in comparison with $LiAlH_4$–transition metal halides. We would like to report on the results of studies concerning the selective conjugate reduction of γ-keto-α,β-unsaturated ketones, such as 2-butene-1,4-diones, with $LiAlH_4$–$SbCl_3$.

The reduction of *trans*-1-phenyl-2-pentene-1,4-dione (**1**), chosen as a representative 2-butene-1,4-dione for this study, with $LiAlH_4$ (LAH)–$SbCl_3$ in various stoichiometric ratios was carried out. The results are summarized in Table 1. At the ratio of enedione **1**, LAH, and $SbCl_3$ (1:1:1, 1:1:3, or 1:3:1), a mixture of 4-hydroxy-1-phenyl-1-pentanone, 1-phenyl-2-pentene-1,4-diol and 1-phenylpentane-1,4-diol and **1** was mainly obtained, accompanied by a small amount of 1-phenylpentane-1,4-dione (**1a**). At a stoichiometric ratio of 1:3:3 or 1:3:4, enedione **1** was reduced to give a conjugate reduction product **1a** in nearly quantitative yield. The optimum conditions for the conjugate reduction of **1** with LAH–$SbCl_3$ found in the present experiments are as follows: i) $SbCl_3$ is essential for effecting a regioselective conjugate reduction. ii) There is need to use either an equal or excess molar equivalent of $SbCl_3$ over LAH in order to suppress the reaction of 1,2-reduction with LAH. iii) There is need to use more than two molar equivalents of LAH and $SbCl_3$ over **1** for obtaining conjugate reduction products in high yield.

The results of a LAH–$SbCl_3$ reduction of other 2-butene-1,4-diones are shown in Table 2. The reductions of *trans*-3-decene-2,5-dione (**2**), ethyl 3-benzoylacrylate (**3**), *trans*- and *cis*-1,4-diphenyl-2-butene-1,4-diones (**5** and **6**), even diethyl azodicarboxylate (**4**) and 3-benzoyl-1-phenyl-2-pentene-1,4-dione (**7**) with LAH–$SbCl_3$ took place to give the corresponding conjugate reduction products in good yields.

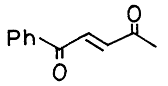
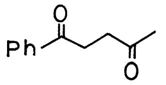
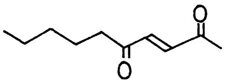
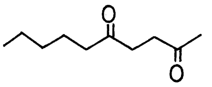
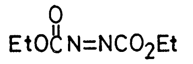
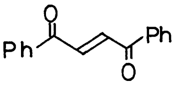
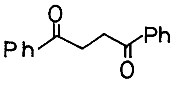
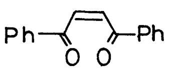
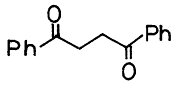
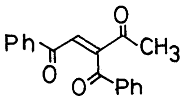
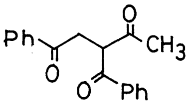
The results of a LAH–$SbCl_3$ reduction of α,β-unsaturated carbonyl compounds are shown in Table 3. The reduction of α,β-unsaturated ketones (**9** and **10**) was not selective, as shown. Only the formyl group of **8** was reduced to a hydroxyl group in 92% yield. The chemoselective reduction of aldehydes in the presence of ketones with this reagent was also examined in the following competition experiments. Equimolar amounts of 3,7-dimethyl-6-octenal and ethyl levulinate were

Table 1. Reduction of *trans*-1-Phenyl-2-pentene-1,4-dione **1** with $LiAlH_4$–$SbCl_3$ in THF at 0 °C for 4 h[a]

Entry	Molar ratio			Products, yield/%[b]			
	Enedione **1**	$LiAlH_4$	$SbCl_3$	1-Phenylpentane-1,4-dione **1a**	Hydroxy compound: Hydroxy ketone **1b**	Hydroxy compound: Diol **1c**	Recovered enedione **1**
1	1	2	0	—	56[c]	38[d]	—
2	1	1	1	32	30[e]	—	33
3	1	1	3	23	—	—	76
4	1	2	2	60	10[c]	—	21
5	1	3	3	84	6[c]	—	—
6	1	3	1	14	42[c]	43[f]	—
7	1	3	9	87	—	—	—
8	1	3	4	93	—	—	—
9	1	0	3	—	—	—	99

a) LAH; 1.0—3.0 mmol; Solvent; 10—15 ml. b) Yield is based on enedione **1** used. c) 4-Hydroxy-1-phenyl-1-pentanone. d) 1-Phenyl-2-pentene-1,4-diol. e) Mixture of **1b** and **1c**. f) Mixture of enediol and saturated diol.

Table 2. Reduction of 2-Butene-1,4-dione with $LiAlH_4$–$SbCl_3$ in THF at 0 °C for 4 h[a)]

Substrate	(S)	Molar ratio S	: LAH	: $SbCl_3$	Products		Yield/%[b)]
	**1**	1	3	3		**1a**[8)]	84
	**2**	1	3	3		**2a**[8,9)]	94
$PhCOCH{=}CHCO_2Et$	**3**	1	3	3	$PhCOCH_2CH_2CO_2Et$	**3a**[8)]	86
 $EtO\overset{\overset{O}{\Vert}}{C}N{=}NCO_2Et$	**4**	1	3	3	 $EtO\overset{\overset{O}{\Vert}}{C}NHNHCO_2Et$	**4a**	81
	**5**	1	3	3		**5a**[12,13)]	78
	**6**	1	3	3		**5a**[12,13)]	81
	**7**	1	2.5	2.5		**7a**	64

a) LAH; 1.0—3.0 mmol; Solvent; 10—15 ml. b) Yield is based on 2-butene-1,4-dione used.

Table 3. Reduction of Carbonyl Compounds with $LiAlH_4$–$SbCl_3$ in THF at 0 °C for 4 h[a)]

Substrate	(S)	Molar ratio S	: LAH	: $SbCl_3$	Products		Yield[b)]/%
$C_6H_5CH{=}CHCHO$	**8**	1	2	2	$C_6H_5CH{=}CHCH_2OH$	**8a**	92
					$C_6H_5CH_2CH_2CH_2OH$	**8b**	7
$C_6H_5CH{=}CHCOCH_3$	**9**	1	3	3	$C_6H_5CH_2CH_2COCH_3$	**9a**	12
					$C_6H_5CH{=}CHCH(OH)CH_3$	**9b**	44
					Recovered	**9**	42
$C_6H_5CH{=}CHCOC_6H_5$	**10**	1	3	3	$C_6H_5CH_2CH_2COC_6H_5$	**10a**	16
					Recovered	**10**	50

a) LAH; 1.0—3.0 mmol; Solvent; 10—15 ml. b) Yield is based on the carbonyl compounds used.

allowed to compete for the reduction with three molar equivalents of LAH–$SbCl_3$. 3,7-Dimethyl-6-octenal was selectively reduced to 3,7-dimethyl-6-octene-1-ol in 70% yield and ethyl levulinate was recovered unchanged. In addition, carbonyl groups of 1-phenylbutane-1,3-dione and 1-phenylpentane-1,4-dione and ester, nitrile, and acetal groups in ethyl levulinate and 4-phenyl-4,4-ethylenedioxybutanenitrile were not affected under the above-mentioned reduction conditions.

On the other hand, the reduction of enedione **1** with LAH–other metal halides such as Cu_2I_2, $CuCl_2$, $AlCl_3$, $FeCl_3$, and $TiCl_4$ gave no 1,4-reduction products, and complex mixture of hydroxy derivatives were obtained under various ratios of LAH and metal halides.

Thus, the reagent LAH–$SbCl_3$ provides a new convenient method for a mild, selective conjugate reduction of 2-butene-1,4-diones. Further application of reduction with LAH–$SbCl_3$ to aldehyde and other functional groups is now in progress.

Experimental

IR spectra were recorded on a JASCO A-100 spectrometer. ^1H NMR spectra were taken on a Hitachi R-24B spectrometer with TMS as an internal standard. The products were identified by spectroscopic data.

General Procedure. To a suspension of LAH (113 mg, 3 mmol) in THF (8 ml) at 0 °C was added $SbCl_3$ (684 mg, 3 mmol) dissolved in THF (2 ml). The resulting mixture was stirred for 5 min at 0 °C, and then 2-butene-1,4-dione (1 mmol) in THF (2 ml) was added. After stirring for 4 h at 0—18 °C, the reaction mixture was treated with 1 M aq Na_2CO_3 and extracted with ethyl acetate. The organic layer was washed by 0.5 M aq HCl and successively saturated aq

NaCl and dried by $MgSO_4$. After removal of the solvent in vacuo, the residue was purified by column chromatography on silica gel (Wakogel C-300) with CCl_4 and $CHCl_3$ (3:1). Conjugate reduction products **1a**—**7a** were obtained in 64—94% yield.

2-Butene-1,4-diones were prepared according to a procedure from the literature.

trans-1-Phenyl-2-pentene-1,4-dione (**1**)[11] and *trans*-3-decene-2,5-dione (**2**) were prepared by pyridinium chlorochromate (PCC) oxidation of the corresponding 2,5-dialkylfuran derivatives.[10]

trans-1,4-Diphenyl-2-butene-1,4-dione (**5**)[11,12] was prepared by Friedel–Crafts acylation of benzene with fumaryl chloride.[14] *cis*-1,4-Diphenyl-2-butene-1,4-dione (**6**)[11,12] and 3-benzoyl-1-phenyl-2-pentene-1,4-dione (**7**) were prepared by oxidation of corresponding furan derivatives with HNO_3 in acetic acid.[15]

3-Benzoyl-1-phenylpentane-1,4-dione (7a): Mp 83—84 °C (from CCl_4); IR (KBr) 1720, 1690, and 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.22 (3H, s), 3.70 (2H, m), 5.30 (1H, t, J=6.0), 7.26—8.26 (10H, m).

***trans*-3-Decene-2,5-dione (2):** Mp 46—47 °C (from hexane); IR (KBr) 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.85 (3H, t, J=7.0), 1.13—2.00 (6H, m), 2.33 (3H, s), 2.47—2.83 (2H, m), 6.70 (2H, s).

3-Benzoyl-1-phenyl-2-pentene-1,4-dione (7): Mp 112—113 °C (from ethanol); IR (KBr) 1685 and 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.35 (3H, s), 7.20—8.10 (11H, m).

References

1) a) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., Menlo Park, California (1972), p. 45; b) E. C. Ashby and B. Cooke, *J. Am. Chem. Soc.*,**90**, 1625 (1968).

2) a) T. Imamoto, T. Takeyama, and T. Kusumoto, *Chem. Lett.*, **1985**, 1491; b) E. C. Ashby and J. J. Lin, *Tetrahedron Lett.*, **1977**, 4481.

3) E. C. Ashby, J. J. Lin, and R. Kover, *J. Org. Chem.*, **41**, 1939 (1976), and references cited therein.

4) T. Tsuda, T. Fujii, K. Kawasaki, and T. Saegusa, *J. Chem. Soc., Chem. Commun.*, **1980**, 1013.

5) a) M. Fieser and L. F. Fieser, "Reagents for Organic Synthesis," John Wiley & Sons,Inc., New York, Vol. 1—13; b) S. S. Pizey, "Synthetic Reagents," John Wiley & Sons,Inc., New York (1974), Vol. 1, p. 101.

6) T.-L. Ho, "Hard and Soft Acids and Bases Principle in Organic Chemisty," Academic Press, New York (1977), p. 93.

7) J. Bottin, O. Eisenstein, C. Minot, and N. T. Anh, *Tetrahedron Lett.*, **1972**, 3015.

8) H. Stetter, *Angew. Chem., Int. Ed. Engl.*, **15**, 639 (1976).

9) H. Stetter and H. Kuhlmann, *Tetrahedron Lett.*, **1974**, 4505.

10) G. Piancatelli, A. Scettri, and M. D'Auria, *Tetrahedron*, **36**, 661 (1980).

11) C.-S. Chien, T. Kawasaki, M. Sakamoto, Y. Tamura, and Y. Kita, *Chem. Pharm. Bull.*, **33**, 2743 (1985).

12) Y. Inamura and Y. Inamura, *Nippon Kagaku Kaishi*, **1985**, 134.

13) Y. Kobayashi, T. Taguchi, T. Morikawa, E. Tokuno, and S. Sekiguchi, *Chem. Pharm. Bull.*, **28**, 262 (1980).

14) R. E. Lutz, "Organic Syntheses," John Wily & Sons, Inc., New York (1955), Coll. Vol. III, p. 248.

15) a) R. E. Lutz and R. J. Rowlett, Jr., *J. Am. Chem. Soc.*, **70**, 1359 (1948); b) R. E. Lutz and F. N. Wilder, *ibid.*, **56**, 978 (1934).