CHEMISTRY LETTERS, pp. 1491-1492, 1985. © 1985 The Chemical Society of Japan

FACILE REDUCTION OF ORGANIC HALIDES AND PHOSPHINE OXIDES WITH $LiAlH_4$-$CeCl_3$

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A new reagent system, $LiAlH_4$-$CeCl_3$, exhibits powerful and characteristic reducing ability. Organic halides including fluorine compounds are smoothly dehalogenated with this reagent. Phosphine oxides are also reduced to phosphines in excellent yields.

In our continuing study on the utilization of cerium metal and its major inorganic salts in organic syntheses,1) a new reducing agent, $LiAlH_4$-$CeCl_3$, has been exploited. In this letter we wish to report the characteristic reducing ability of the reagent.

Our idea behind these experiments is based on the assumption that the extremely "hard" Lewis acid character of cerium cation might so perturb halogen and oxygen functions as to be reduced with $LiAlH_4$-$CeCl_3$.2) Our initial trial was conducted with the reductive dehalogenation of chlorine and fluorine compounds. After various screening of the reaction conditions, it was found that aliphatic and aromatic halides were smoothly reduced with $LiAlH_4$-$CeCl_3$(3:1) in 1,2-dimethoxyethane(DME) or THF at reflux.3)

Several examples are listed in Table 1. A characteristic feature of this method is that not only chlorine but also fluorine compounds are readily subjected to reductive dehalogenation.4) This method may be applicable to the reduction of extremely toxic organic halides such as polychlorobiphenyl(PCB). The reaction with $LiAlD_4$-$CeCl_3$ is also worthy to mention. The products isolated contained no detectable amounts of deuterium (Entries 4 and 10). These results clearly indicate that the reduction does not proceed through direct hydride attack but via a radical intermediate which abstracts a hydrogen atom from the solvent DME or THF. The actual reducing agent may be low-valent cerium which is generated by the reaction of $CeCl_3$ with $LiAlH_4$ at refluxing temperature.

Next, we tried the reduction of phosphine oxides using the $LiAlH_4$-$CeCl_3$ reagent system. The results are added in Table 1. It is noted that phosphine oxides were rapidly deoxygenated under mild conditions to afford the corresponding phosphines in excellent yiels. Unfortunately, however, the reduction of optically active (S)-(o-methoxyphenyl)methylphenylphosphine oxide proceeded with predominant racemization (Entry 14).

This $CeCl_3$-assisted reaction is favorably compared with the previously existing methods5) and is especially suitable for the reduction of sterically crowded phosphine oxides.

Table 1. Reduction of Organic Halides and Phosphine Oxides with $LiAlH_4$-$CeCl_3$

Entry	Substrate	Conditions a)	Product	Yield/ % b,c)
1	$CH_3(CH_2)_{11}F$	THF, reflux, 3 h	$C_{12}H_{26}$	90 (>99)
2	1-Fluoronaphthalene	DME, reflux, 3 h	Naphthalene	94 (>99)
3 d)	″	″	″	0
4	″	″ e)	″ f)	92
5	2-Fluorobiphenyl	DME, reflux, 5 h g)	Biphenyl	94 (98)
6	1-Chloronaphthalene	THF, reflux, 3 h	Naphthalene	95 (>99)
7 d)	″	″	″	37
8	4,4'-Dichlorobiphenyl	DME, reflux, 3 h	Biphenyl	92 (>99)
9	2,4-Dichlorophenol	THF, reflux, 20 h	4-Chlorophenol	81
10	″	″ e)	″ f)	84
11	Ph_3PO	THF, 40 °C, 0.5 h h)	Ph_3P	95
12 d)	″	″ h)	″	trace
13	$Ph_2P(O)CH_3$	″ h)	Ph_2PCH_3	98
14	(<u>S</u>)-(<u>o</u>-$CH_3OC_6H_4$)(Ph)P(O)CH_3 i)	″ h)	(<u>o</u>-$CH_3OC_6H_4$)(Ph)PCH_3 j)	90
15	Ph(1-$C_{10}H_7$)P(O)CH_3	″ h)	Ph(1-$C_{10}H_7$)PCH_3	87
16	[2,4,6-(<u>i</u>-Pr)$_3C_6H_2$](Ph)P(O)CH_3	″ h)	[2,4,6-(<u>i</u>-Pr)$_3C_6H_2$](Ph)PCH_3	89

a) A molar ratio of 1:4.5:1.5 substrate/$LiAlH_4$/$CeCl_3$ was used unless otherwise stated. b) Isolated yield. c) The figures in parentheses indicate the yields determined by GLC. d) The reaction was carried out in the absence of $CeCl_3$ under the same conditions. e) $LiAlD_4$ was used in place of $LiAlH_4$. f) The product was identified by ^1H-NMR and mass spectra. g) Under irradiation with a 200W W-lamp. h) A molar ratio of 1:2:1.5 phosphine oxide/$LiAlH_4$/$CeCl_3$ was used. The reaction was quenched with water, and the product was extracted with benzene and was purified by chromatography on a short column of silica gel using benzene as the eluant. i) 93% ee. j) ≈0% ee.

References

1) T. Imamoto, Y. Sugiura, and N. Takiyama, Tetrahedron Lett., 25, 4233 (1984); T. Imamoto, T. Kusumoto, Y. Tawarayama, Y. Sugiura, T. Mita, Y. Hatanaka, and M. Yokoyama, J. Org. Chem., 49, 3905 (1984) and references cited therein.

2) The use of transition metal halide-$LiAlH_4$ reagent system in organic syntheses has been reported. T. Mukaiyama, M. Hayashi, and K. Narasaka, Chem. Lett., 1973, 291; M. Sato and K. Oshima, ibid., 1982, 157 and references cited therein.

3) General procedure for the dehalogenation: Powdered cerium chloride ($CeCl_3 \cdot 7H_2O$) (560 mg, 1.5 mmol) was dried in vacuo at 135-140 °C for 2 h, and cooled to room temperature. Dry DME or THF (3 ml) was added under argon and the suspension was stirred for 1 h. Substrate (1 mmol) and $LiAlH_4$ (4.5 mmol) were added and the mixture was refluxed for 3 h. The reaction mixture was worked up in the usual manner and the product was isolated by preparative layer chromatography on silica gel.

4) Ohsawa et al. reported the reductive defluorination of aliphatic fluorine compounds with potassium-crown ether. T. Ohsawa, T. Takagaki, A. Haneda, and T. Oishi, Tetrahedron Lett., 22, 2583 (1981).

5) Fr. Hein, K. Issleib, and H. Rabold, Z. Anorg. Chem., 287, 208 (1956); L. Horner, H. Hoffmann, and P. Beck, Chem. Ber., 91, 1583 (1958); K. Issleib and G. Grams, Z. Anorg. Allg. Chem., 299, 58 (1959).

(Received July 8, 1985)