SYNLETT
Spotlight 134

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Aluminum Hydride

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Krishnarao Lopinti was born in Srikakulam, Andhra Pradesh in India in 1978. He obtained his B.Sc. (2000) from Acharya Nagarjuna University and M.Sc. (2002) in chemistry from the University of Hyderabad. After qualifying for a CSIR Junior Research Fellowship through a national search examination CSIR-JRF, he began Ph.D. studies under the supervision of Dr P. Radha Krishna at Indian Institute of Chemical Technology, Hyderabad, India. His research interests are: synthesis of chiral drug molecules/natural products by using asymmetric synthesis/chiron approach, developing synthetic methodologies, asymmetric Baylis–Hillman reaction and its applications.

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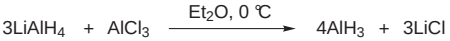
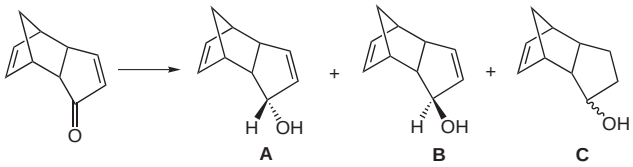
Introduction

A diethyl ether solution of three equivalents of lithium aluminum hydride with one equivalent of aluminum chloride generates a mild reducing hydride known as 'Aluminum Hydride' (AlH_3).[1] This reagent is very useful in synthetic organic chemistry and is easily prepared in situ and used immediately. Lithium aluminum hydride is a powerful reducing agent that can reduce several functional groups. By minimizing its reducing power, selective functional groups can be reduced. In this regard, mixed hydrides have gained a lot of interest in hydride chemistry. Adding a Lewis acid could decrease the reducing power of lithium aluminum hydride. AlH_3 reduces a wide variety of functional groups.[1] These include aldehydes, ketones,[2,3] quinines, carboxylic acids, anhydrides, acid chlorides, esters, and lactones from which the corresponding alcohol is isolated as product. Similarly, amides, nitriles, oximes and isocyanates are reduced to amines. However, nitro compounds are inert to AlH_3. Interestingly sulfides and sulfones are unreactive but disulfides and sulfoxides can be reduced. Tosylates are not reduced.



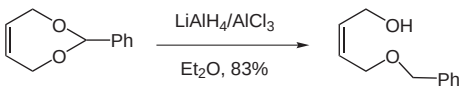
Abstracts

(A) *Reduction of α,β-unsaturated carbonyls and esters*: The conversion of α,β unsaturated ketones, aldehydes, and esters into allylic alcohols can be carried out with very good selectivity using AlH_3.[4] However, DIBAL is a reagent of choice for this transformation but is costly.[4a] Carboxylic acids and esters are rapidly reduced by AlH_3 than $LiAlH_4$ in presence of halides and nitro group.[5]

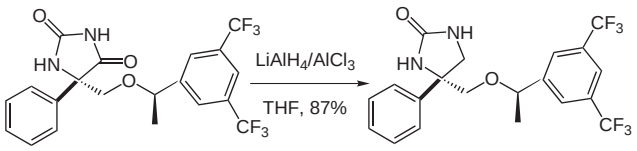


	A	B	C
$LiAlH_4$	65%	17%	18%
$LiAlH_4/AlCl_3$	100%	–	–
$NaBH_4$/MeOH	–	–	100%

(B) *Reduction of acetals*: Cyclic acetals can be reduced to the half protected diols, which has wide applications in carbohydrate chemistry. For instance, acetals (benzylidene derivative) can be selectively reduced to a monobenzylated diol.[6]



(C) *Reduction of amides*: During the reduction of amides to amine, there is a competition between C–O and C–N bond and the cleavage depends upon the reaction conditions. This complication can be avoided with AlH_3. A quantitative yield of amine is obtained within a short reaction time. Conjugated amine can be cleanly reduced to allylic amines, whereas $LiAlH_4$ reduces also the conjugated double bond.[7] Reduction of β-lactams to azetidines can be accomplished with AlH_3[8] while ring opening was observed with $LiAlH_4$.



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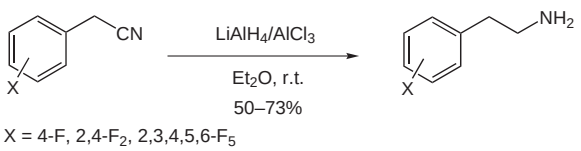
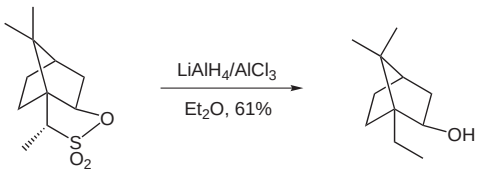
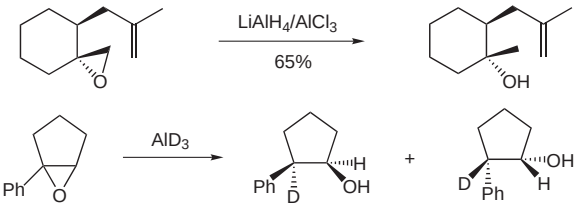
(D) *Reduction of nitriles*: The less basic AlH_3 appears to be better than $LiAlH_4$ for reducing nitriles to amines.[7]



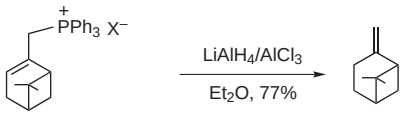
(E) *Desulfurisation*: Desulfurisation of sultones is rapid and proceeds in good yields with AlH_3, while $LiAlH_4$ affords poor yields with long reaction times.[9]



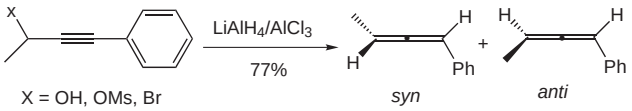
(F) *Epoxide ring opening*: With most epoxides, hydride attack occurs at the least sterically hindered side to give the corresponding alcohol.[10] However due to the electrophilic nature of AlH_3 compared to $LiAlH_4$, it is possible for ring opening to occur at the more hindered side. With phenyl substituted epoxides mechanistic studies have shown that attack at benzylic carbenium ion or 1,2-hydride shift followed by hydride attack gives products with the same regiochemistry but with different stereochemistry.[7,11] The stereoselectivity of AlH_3 mediated epoxide ring opening reaction has been studied in depth.[12]



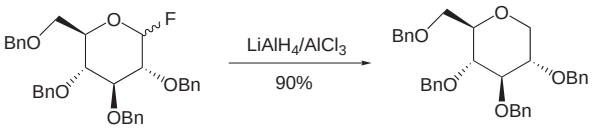
(G) *S_N2' allylic rearrangements*: Displacement of good leaving group to give the rearranged allylic system can be carried out with AlH_3.[13] This reaction appears not to be sterically demanding as a variety of displacements are possible.



(H) *Preparation of allenes*: Preparation of allenes from propargylic system can also be accomplished.[13] Most systems show a preference for syn elimination. However, mesylates prefer an anti mode of elimination. This same procedure has been used to prepare fluoroallenes.[14]



(I) *Miscellaneous*: Though alkyl halides are usually inert to AlH_3, facile reduction of cyclopropyl halides to cyclopropanes[15] and glycosyl fluorides to tetrahydropyrans is known.[16]



References

(1) Finholt, A. E.; Bond, A. C.; Schlesinger, H. I. *J. Am. Chem. Soc.* **1947**, *69*, 1199.
(2) (a) Guyon, R.; Villa, P. *Bull. Soc. Chim. Fr.* **1977**, 152. (b) Martinez, E.; Muchowski, J. M.; Velarde, E. *J. Org. Chem.* **1977**, *42*, 1087.
(3) Corey, E. J.; Cane, D. *J. Org. Chem.* **1971**, *36*, 3070.
(4) (a) Wilson, K. E.; Seidner, R. T.; Masamune, S. *J. Chem. Soc., Chem. Commun.* **1970**, 213. (b) Williams, H. J. *Tetrahedron Lett.* **1975**, 1271. (c) Krishna, P. R.; Krishnarao, L.; Kannan, V. *Tetrahedron Lett.* **2004**, *45*, 7847.
(5) Nung, M. Y. *J. Am. Chem. Soc.* **1966**, *88*, 1464.
(6) Sakairi, N.; Tokura, S.; Kuzuhara, H. *Carbohydr. Res.* **1996**, *291*, 53.
(7) (a) Ashby, E. C.; Sanders, J. R.; Claudy, P.; Schwarts, P. *J. Am. Chem. Soc.* **1973**, *95*, 6485. (b) Brown, H. C.; Nung, M. Y. *J. Am. Chem. Soc.* **1966**, *88*, 1464. (c) Das, B. K.; Shibata, N.; Takaeuchi, Y. *J. Chem. Soc., Perkin Trans. 1* **2002**, 197.
(8) Jackson, M. B.; Mander, L. N.; Spotswood, T. M. *Aust. J. Chem.* **1983**, *36*, 779.
(9) (a) Wolinsky, J.; Marhenke, R. L.; Eustace, E. J. *J. Org. Chem.* **1973**, *38*, 1428. (b) Smith, M. B.; Wolinsky, J. *J. Org. Chem.* **1981**, *46*, 101.
(10) Maruoka, K.; Saito, S.; Ooi, T.; Yamamaoto, H. *Synlett* **1991**, 255.
(11) Lansbury, P. T.; Scharf, D. J.; Pattison, V. A. *J. Org. Chem.* **1967**, *32*, 1748.
(12) Elsenbaumer, R. L.; Mosher, H. S.; Morrison, J. D.; Tomaszewski, J. E. *J. Org. Chem.* **1981**, *46*, 4034.
(13) Claesson, A.; Olsson, L. I. *J. Am. Chem. Soc.* **1979**, *101*, 7302.
(14) Castelhano, A.; Krantz, A. *J. Am. Chem. Soc.* **1987**, *109*, 3491.
(15) Muller, P. *Helv. Chim. Acta* **1974**, *57*, 407.
(16) Nicolaou, K. C.; Dolle, R. E.; Chucholowski, A.; Randal, J. L. *J. Chem. Soc., Chem. Commun.* **1984**, 1153.