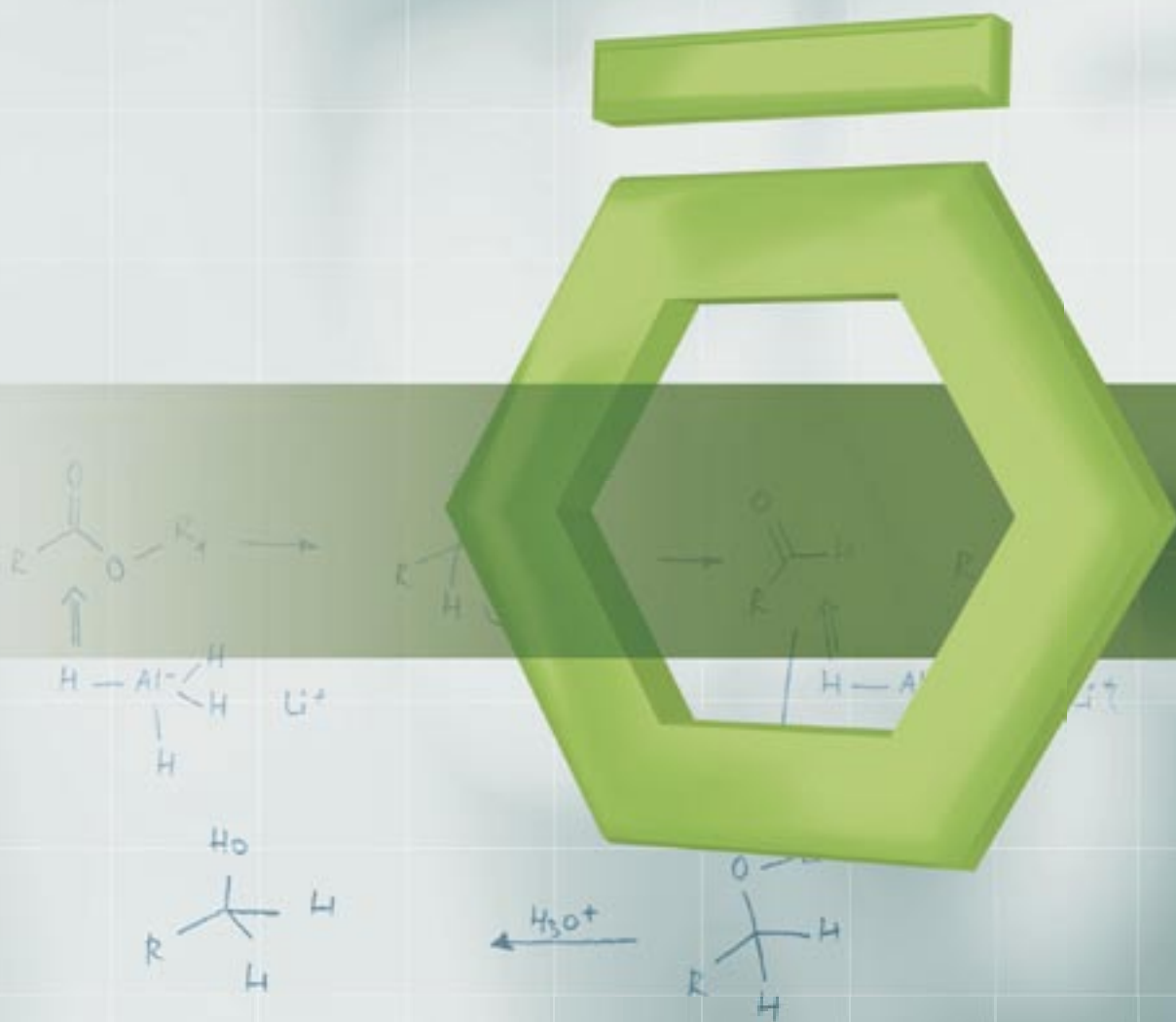


ALUMINIUM HYDRIDES AND BOROHYDRIDES





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1 - Introduction

The importance of organo-boron and organo-aluminium compounds for science and technology has resulted in three Nobel-prizes for Herbert C. Brown for his work on hydroboration¹, for Giulio Natta and Karl Ziegler for their work on olefin polymerization² and for William Nunn Lipscomb for his work on the chemical bonding in boranes³.

Organoboron compounds and organoaluminium compounds have a wide range of applications:

- Borohydrides and aluminium hydrides can act as reducing agents for carbonyl compounds
- They are reagents for the widely used hydroboration and hydroalumination
- They can act as Lewis acids
- And as alkylating agents for aldehydes with alkyl aluminium compounds⁴

The first aluminium-organic compound was synthesized in 1859 by W. Hallwachs and A. Schafarik⁵.

¹ Nobel prize 1979 with Georg Wittig.

² Nobel prize 1963.

³ Nobel prize 1976.

⁴ S. Flemming, J. Kabbara, K. Nickisch, H. Neh, J. Westermann, *Synthesis* 1995, 317.

⁵ W. Hallwachs, A. Schafarik, *J. Liebigs Ann. Chem* 109, 206 (1859).



2 - Synthesis and Properties

Trimethylaluminium and **triethylaluminium** can be made by the reaction of aluminium metal with methyl chloride, sodium chloride and sodium:

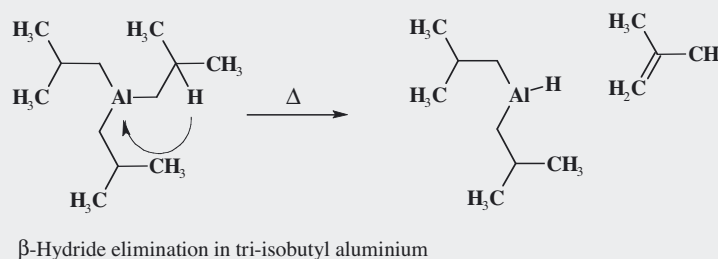


- $\text{Me}_2\text{Al}_2\text{Cl}_4$ precipitates after addition of 2 equivalents of sodium chloride as $\text{Na}[\text{MeAlCl}_3]$
- The remaining $\text{Me}_4\text{Al}_2\text{Cl}_2$ is reduced with sodium metal:
 $3 \text{ Me}_4\text{Al}_2\text{Cl}_2 + 6 \text{ Na} \rightarrow 2 \text{ Al}_2\text{Me}_6 + 6 \text{ NaCl} + 2 \text{ Al}$
- or with aluminium, hydrogen and ethylene according to the following scheme (Ziegler Direct Process):
 $\text{Al} + 1\frac{1}{2} \text{ H}_2 + 2 \text{ Et}_3\text{Al} \rightarrow 3 \text{ Et}_2\text{AlH} \quad (80^\circ\text{C} - 160^\circ\text{C}, 100\text{-}200 \text{ bar})$
 $3 \text{ Et}_2\text{AlH} + 3 \text{ Ethylene} \rightarrow 3 \text{ Et}_3\text{Al} \quad (80\text{-}110^\circ\text{C}, 1\text{-}10 \text{ bar})$

On laboratory-scale aryl and alkylaluminium compounds can be made by metal-exchange reactions⁶ $3 (\text{C}_6\text{H}_5)_2\text{Hg} + 2 \text{ Al} \rightarrow 3 \text{ Hg} + 2 (\text{C}_6\text{H}_5)_3\text{Al}$

or by a transmetallation- reaction
 $\text{AlCl}_3 + 3 \text{ MeLi} \rightarrow \text{Al}_3\text{Me} + 3 \text{ LiCl}$.

The very useful reducing agent Diisobutylaluminium hydride (DIBAL-H, *vide infra*) is made by β -hydride elimination of Triisobutylaluminium:



Boranes were first systematically described by Alfred Stock in 1912 and the discovery of the unusual structure of boranes resulted in the Nobel-Prize for William Nunn Lipscomb^{3,7}. The remarkable chemical behavior of boranes was thoroughly discovered by H.C. Brown and co-workers in the 1960's and the following decades. This work^{8,9} resulted in a Nobel-Prize in 1979.

⁶ Organic Syntheses, Coll. Vol. 5, p.1116; Vol. 45, p.107.

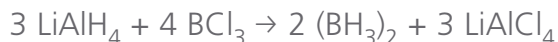
⁷ A nice essay about the „History Of Diborane“ in: P. Laszlo, Angew. Chem. 112 (2000) 2151.

⁸ H.C. Brown, „Organic Synthesis Via Boranes“, John Wiley & Sons, New York 1975.

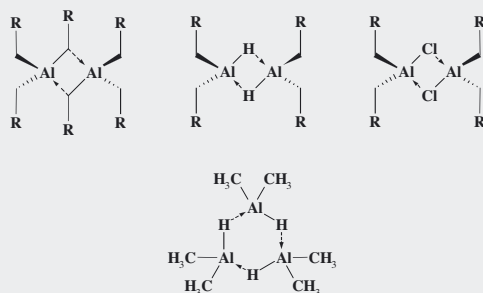
⁹ H.C. Brown, „Hydroboration“, W.A. Benjamin, Inc. New York 1962.



Boranes were originally produced by the hydrolysis of magnesium boride^{10,11}. This process produced mainly tetraborane (B₄H₁₀). Diborane was accessible through the pyrolysis of the tetraborane. The modern synthesis of boranes used the reaction of metal hydrides with boron halides in ethereal solution^{12,13}.



Tri-coordinated aluminium and boron compounds like trialkylborane are electron deficient species (6 valence electrons) and hence Lewis-acidic compounds.



Trialkylaluminium compounds and dialkylaluminium hydrides are usually dimer or trimer with alkyl- and hydride-bridges, while alkylaluminium halides are normally associated through halide-bridges. Even triaryl-aluminium compounds are dimer with two bridging phenyl-groups¹⁴.

Boranes show remarkably complex structures¹⁵ with hydrogen bridges, while boron-trihalides are monomeric species¹⁵. Aluminium chloride is polymeric at ambient temperature but forms dimeric Al₂Cl₆ upon melting.

Mono- and dialkylboranes like 9-borabicyclo[3.3.1]nonane form dimeric species¹⁶, while trialkylboranes are trigonal-planar monomers¹⁷.

Since trialkylaluminium- or trialkylboron compounds are Lewis-acidic they tend to form stable adducts with Lewis bases like amines, ethers and thioethers. These complexes are far more stable and easy to handle. Not surprisingly numerous of these compounds are commercially available and offer a convenient approach to borane-chemistry.

Products from Acros Organics	
Borane-tert-butylamine complex, powder 95%	17730
Borane-tert-butylamine complex, pellets	18922
Borane-N,N-diethylaniline complex 97%	17677
Borane-dimethylamine complex 98+%	17731
Borane-methyl sulfide complex 94%	17706

¹⁰ A.E. Newkirk, D.T Hurd, J. Am. Chem. Soc., 1955, 241.

¹¹ C.F. Lane, Chem Rev. 1976, 773.

¹² Römpp, Chemielexikon Georg Thieme Verlag, Stuttgart 1995.

¹³ Hollemann, Wiberg, Lehrbuch der anorganischen Chemie, Walter de Gruyter, Berlin 1985.

¹⁴ C.T. Sirimanne, J.E. Knox, M.J. Heeg, H.B. Schlegel, and C.H. Winter, J. Am. Chem. Soc. 125 (2003) 11152.

¹⁵ N.N. Greenwood, A. Earnshaw, Chemistry of the elements, Pergamon Press, Oxford 1984; A.F. Hollemann, N. Wiberg, Lehrbuch der anorganischen Chemie, deGruyter, Berlin 1985.

¹⁶ Organic Syntheses, Coll. Vol. 9, p.95; Vol. 70, p.169.

¹⁷ N. Krause, Metallorganische Chemie, Spektrum-Verlag, Heidelberg 1996.



Borane-methyl sulfide complex, 1M solution in methylene chloride	18561
Borane-methyl sulfide complex, 2M solution in tetrahydrofuran	18507
Borane-morpholine complex 97%	17729
Borane-pyridine complex 95%	17701
Borane-tetrahydrofuran complex, 1M solution in THF, stabilized	17508
Borane-triethylamine complex 99%	40273
Borane-trimethylamine complex 98%	40274
Borane-triphenylphosphine complex 97%	22300

They can also form complex alkyl-compounds ("ate"-complexes) or complex hydrides like sodium tetraphenylborate, lithium aluminium hydride or sodium borohydride

Products from Acros Organics	
Sodium tetraethylborate 97%	36388
Tetraphenylboron sodium, p.a.	13852
Tetraphenylboron sodium, reagent ACS	42445

Complex aluminium hydrides and borohydrides are important reducing agents and their synthetic properties are discussed in the following chapters in this brochure.

They have often common structural elements; a four membered ring of Li_2H_2 or a eight-membered ring of $(\text{Li-H-Al-H})_2$ units¹⁸.

Vigorous reaction with oxygen and water

Alkylboranes and alkylaluminium compounds are usually extremely sensitive to water and air and can react violently. Many compounds, especially those with a high metal content are pyrophoric and have to be handled with special caution. An overview on the pyrophoricity of metal alkyls in different solvents is available from Akzo Nobel¹⁹.

Stability

Tri(n-alkyl)aluminium compounds are thermally relatively stable, β -hydride elimination usually starts at temperature above 100°C. β -branched alkyl-aluminium compounds are much less stable towards β -hydride-elimination; here this reaction becomes significant at ~50°C²⁰.

¹⁸ M. Veith, P. König, A. Ramno, V. Huch, Angew. Chem. 117 (2005) 6122.

¹⁹ Akzo Nobel, Technical Bulletin, Pyrophoricity of Metal Alkyls, January 2003.

²⁰ Akzo Nobel product brochure.



3 - Chemistry

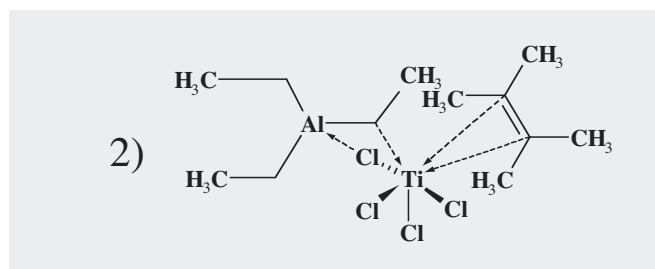
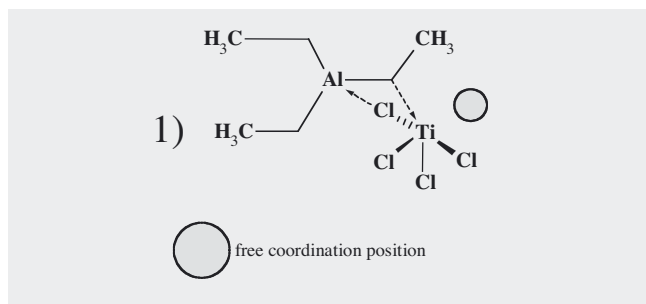
3.1 Alkylaluminium compounds as Ziegler²¹-Natta²² co-catalysts

In 1955 Karl Ziegler at the "Max-Planck-Institut für Kohleforschung" in Mülheim an der Ruhr, Germany discovered that a catalyst consisting of titanium tetrachloride and diethylaluminium chloride could polymerize ethylene at normal pressure and room temperature to yield polyethylene. The previous process for the synthesis of polyethylene used pressures up to 2000 atmospheres and temperatures up to 200°C.

Shortly after the discovery of Karl Ziegler in Mülheim, Giulio Natta of the "Istituto di Chimica Industriale del Politecnico" in Milan, Italy described the polymerization of propylene catalyzed by a mixture of titanium tetrachloride and triethylaluminium to yield highly isotactic polypropylene with superior density, hardness and toughness.

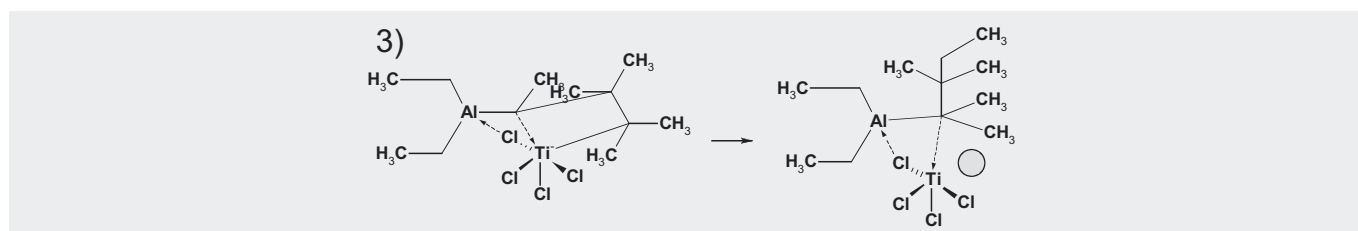
The Ziegler-Natta²³ polymerization is used mainly for the production of isotactic or syndiotactic polypropylene and linear polyethylene (HDPE) at low temperature and pressure. The catalyst is a system of two components, where a titanium or vanadium halogenide (TiCl_3 , TiCl_4 or VCl_4) acts as main catalyst and an alkyl-aluminium compound (Et_2AlCl or Et_3Al) acts as co-catalyst.

Catalyst and co-catalyst form a complex with a free coordination position (1).



The free coordination at the catalyst is filled by the pi-system of the monomer (2)

The pi-bonded olefin inserts in the next step into the existing titanium-carbon bond and (3) the coordination position at the catalyst is free for the next monomer and the cycle to start again.



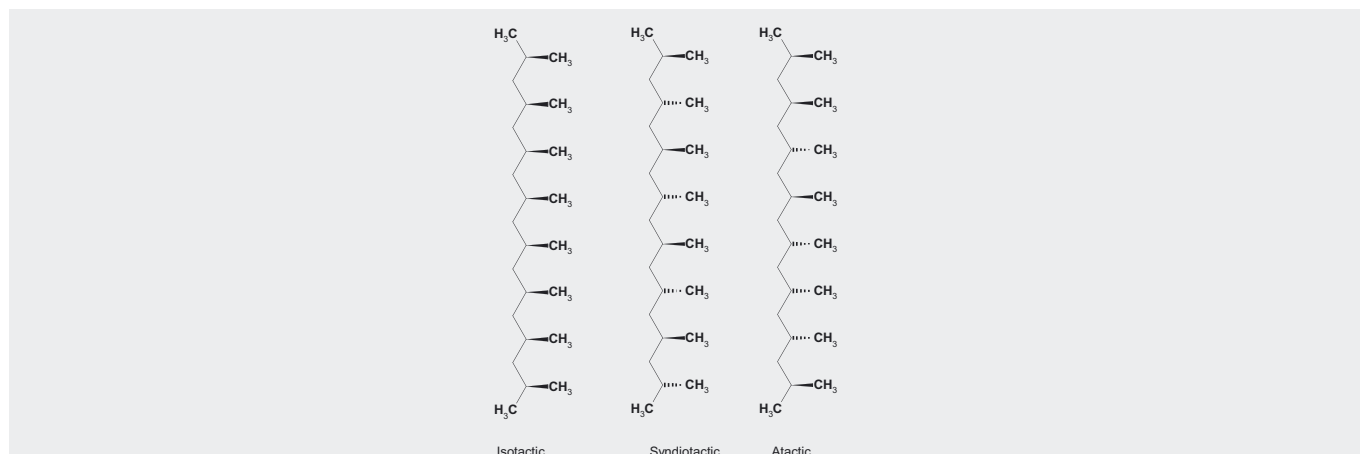
²¹ K. Ziegler, E. Holzkamp, H. Breil and H. Martin, *Angew. Chem.* 67 (1955) 541.

²² G. Natta, P. Pino, P. Corradini, F. Danusso, E. Mantica, G. Mazzanti, G. Moraglio, *J. Am. Chem. Soc.*, 77 (1955) 1708.

²³ G. Wilke: *Angew. Chem. Int. ed. engl.* 42 (2003) 5000.



The tacticity of the resulting polymer is influenced by the applied catalytic system:



While the catalytic system described above gives **isotactic polypropylene** the system made from vanadium tetrachloride and diethylaluminium chloride yields **syndiotactic polypropylene**.

Products from Acros Organics	
Titanium(III)chloride 98%, Al reduced	33152
Titanium(III) chloride, 30 wt% solution in 2N hydrochloric acid	23550
Titanium(IV) chloride 99.90%	19723
Titanium(IV) chloride, 1M solution in dichloromethane	37774
Titanium(IV) chloride, 1M solution in toluene	37816
Vanadium(IV) chloride 99+%	29969
Diethylaluminium chloride, 0.9M solution in toluene	38115
Diethylaluminium chloride, 1.1M solution in toluene	18544
Diethylaluminium chloride, 1M solution in hexanes	19952

Many other catalyst systems based on the Ziegler-Natta catalyst have been developed in the past years which allow a selective fine tuning of the olefin-polymerization^{24,25,26}. Especially the polymerization with metallocenes and methylaluminumoxane as co-catalysts resulted in a large number of polymers with new and unique properties²⁵.

Products from Acros Organics	
Bis(cyclopentadienyl)dimethyltitanium, 5 wt% in toluene	30176
Bis(cyclopentadienyl)dimethylzirconium	34789
Bis(cyclopentadienyl)titanium(III) chloride 96%	37574
Bis(cyclopentadienyl)titanium dichloride 99%	37246
Bis(cyclopentadienyl)titanium dichloride 97%	21576
Bis(cyclopentadienyl)vanadium 95%	35340
Bis(cyclopentadienyl)vanadium dichloride 95%	35341

²⁴ H. Sinn, W. Kaminsky, Adv. Organometal. Chem. 18 (1980) 99; H. Sinn, W. Kaminsky, H. Vollmer, R. Woldt, Angew. Chem. Int. Ed. Engl. 19 (1980) 390.

²⁵ W. Kaminsky, Polymerization Catalysis, in: Basic Principles in Applied Catalysis, M. Baerns (ed.), Springer press, Berlin 2004, 403-440.

²⁶ H.H.-Brintziger, D. Fischer, R. Mülhaupt, B. Rieger, R. Waymouth, Angew. Chem. 107 (1995) 1225.



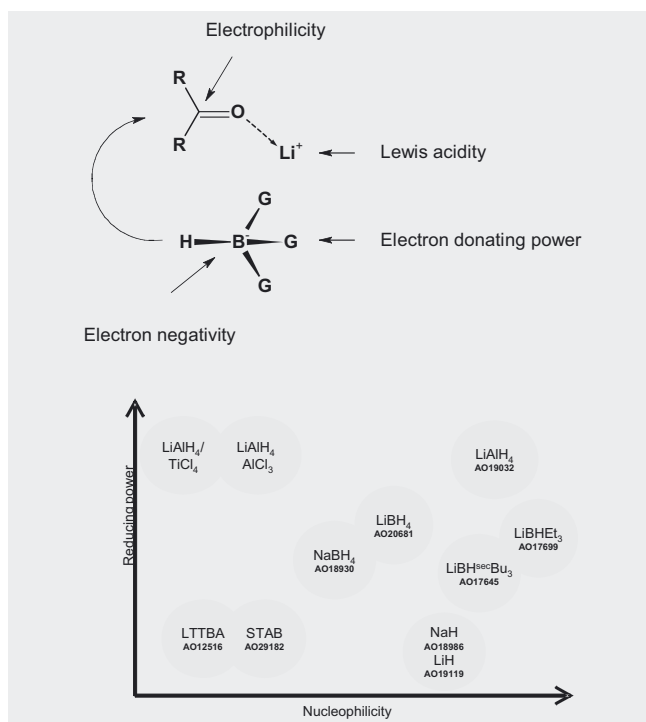
3.2 Complex aluminium hydrides and borohydrides as reducing agents²⁷

The selective reduction of carbonyl-groups is amongst the most common synthetic transformations in organic chemistry.

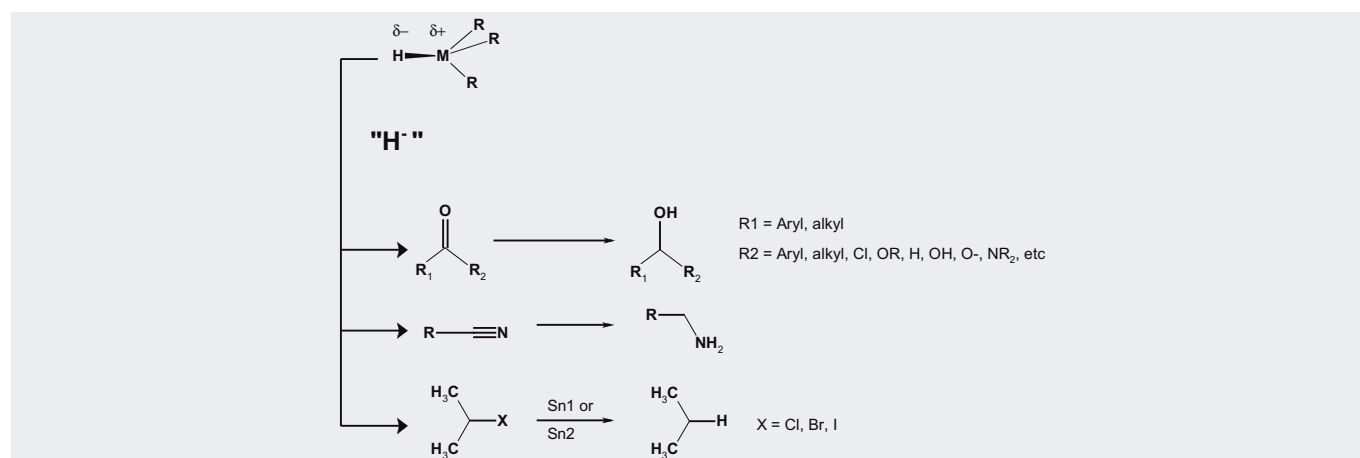
Complex hydrides of boron and aluminium are very useful reagents to accomplish these transformations for a wide number of substrates and with a broad variety of selectivities and reactivities²⁸.

The reactivity of the metal hydride is influenced by the following factors:

- electro-negativity of the central metal (Al > B)
- electron donating groups on the central metal
- Lewis acidity of the counter ion
- polarity of the reducible functional group
- sterical demand of the reagent



The general reaction mechanism is a nucleophilic attack of a hydride ion at a suitable functional group as sketched in the following scheme:



The following chapters of this brochure will give an overview of the most commonly used aluminium hydrides and borohydrides.

²⁷ J. Seyden-Penne, Reductions by the Alumino- and Borohydrides in Organic Synthesis.

²⁸ N.M. Yoon, Pure. Appl. Chem. 68 (1996) 843.



3.3 The parent compounds lithium aluminium hydride and sodium borohydride

The two parent compounds lithium aluminium hydride and sodium borohydride were both first synthesized in the laboratories of Prof. Schlesinger at the University of Chicago²⁹.

3.3.1 Lithium aluminium hydride³⁰ (LAH) is made from aluminium chloride and lithium hydride^{29,13} according to $4 \text{ LiH} + \text{AlCl}_3 \rightarrow \text{LiAlH}_4 + 3 \text{ LiCl}$.

LAH³¹ is easily soluble in ethereal solvents³² as shown in the following table, but reacts violently with protic solvents. THF and Diethylether are the most common solvents for reactions with LAH.

Solubility (g/100g solvent) of LiAlH ₄ at 25°C			
Diethyl ether	39	THF	15
THF/Toluene (70:30)	17	MTBE	0,6
THF/Toluene (15:85)	5	1,4-Dioxane	0.1
THF/MTBE (25:75)	12	Di-n-butylether	2
Ethylenglycoldimethylether	7		
Diethylenglycoldimethylether	5		
Triethylenglycoldimethylether	2		

It is a white, fine crystalline powder, which can turn grey during storage due to the formation of trace amounts of aluminium or oxidized material. This can also be the reason for the turbidity of some solutions. The reducing power of LiAlH₄ is usually not effected by these traces.

LAH reacts violently with water and forms a large amount of highly flammable hydrogen-gas during this reaction: $\text{LiAlH}_4 + 4 \text{ H}_2\text{O} \rightarrow \text{LiOH} + \text{Al(OH)}_3 + 2 \text{ H}_2$. This reaction is also very exothermic ($\Delta H^\circ_{298} = -714 \text{ kJ/mol}$)³² so the hydrogen can ignite spontaneously. **When handling Lithium aluminium hydride make sure to avoid accidental contact with water.**

LAH is a very powerful but not very selective reducing agent. It reduces carboxylic acids and esters, amides, epoxides,³³ lactones, aldehydes and ketones³⁴ readily to the corresponding alcohols and amines. Also sulfones,³⁵ sulfoxides³⁵ and sulfonylhalides are reduced to the thioethers and mercaptanes, alkylhalides to alkanes,^{36,37,38,39} aromatic nitro- and nitroso-compounds to azo-compounds while aliphatic nitro- and nitroso-compounds are reduced to amines.

Also many other functional groups are reduced: i.e. ortho-esters to acetals⁴⁰, azides, isonitriles, isocyanates and isothiocyanates etc.

²⁹ H.C. Brown Nobel Lecture 1979

³⁰ A.E. Finhold, A.C. Bond, H.I. Schlesinger, J. Am. Chem. Soc. 69 (1947) 1199.

³¹ Fieser & Fieser: Reagents for organic synthesis Vol 1, J. Wiley & Sons New York 1967, p 582.

³² Product-brochure of Chemetall GmbH October 2000.

³³ B.C. Hartman, B. Rickborn, J. Org. Chem. 37 (1972) 4246.

³⁴ J. March, Advanced Organic Chemistry, Fourth Edition, John Wiley & Sons 1992, p 910.

³⁵ A.G. Anastassiou, J.C. Wetzell, B.Y.-H. Chao, J. Am. Chem. Soc. 97 (1975) 1124.

³⁶ S. Krishnamurthy, H.C. Brown, J. Org. Chem. 47 (1982) 276; S. Krishnamurthy, H.C. Brown, J. Org. Chem. 45 (1980), 849.

³⁷ C.W. Jefford, D. Kirkpatrick, F. Delay, J. Am. Chem. Soc. 94 (1972) 8905.

³⁸ J.S. Kim, J.H. Choi, H.D. Kim, J.H. Yun, C.Y. Joo, D.J. Baek, Bull. Korean Chem. Soc. 20 (1999) 237.

³⁹ E.C. Ashby, C.O. Welder, F. Doctorovich Tetrahedron Lett. 34 (1993) 7235.

⁴⁰ C.J. Claus, J.L. MORGANTHAU, J. Am. Chem. Soc. 73 (1951) 5005.

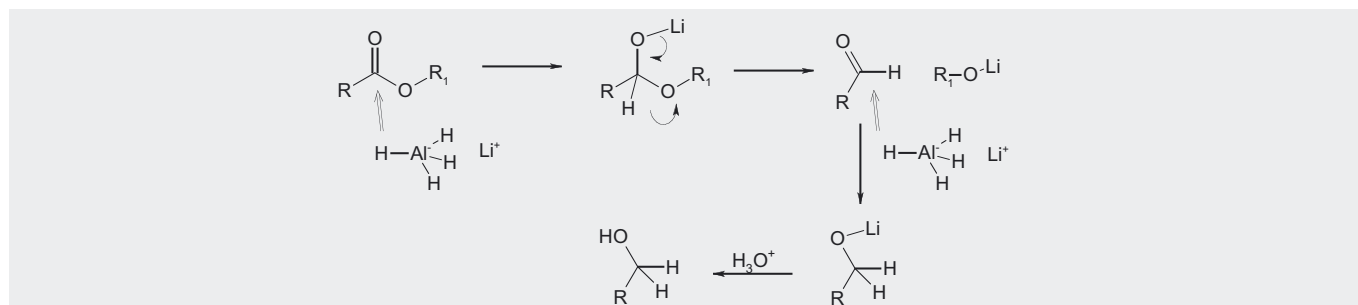


Tosylates are reduced by LAH to the alkanes, which is a facile method for the deoxygenation of alcohols⁴¹ although cyclic or sterically bulky tosylates can give elimination products.

The ease of reduction of different substrates with Lithium aluminium hydride is given in the following table:

Educt	Product	Ease of reduction
Aldehyde	to 1°-Alcohol	most readily reduced
Ketone	to 2°-Alcohol	
Acid chloride	to 1°-Alcohol	
Lactone	to Diol	
Epoxide	to Alcohol	
Carboxylic acid	to Alcohol	
Carboxylate	to Alcohol	
Amide	to Amine	
Nitrile	to Amine	
Nitro	to Azo	most difficult to reduce
Isolated double-bond		not reactive

The mechanism of the reduction involves a nucleophilic attack of hydride to the substrate, as shown for an ester in the following scheme.



It has to be taken into consideration for the stoichiometry that all four hydrogen-atoms are used for the reduction⁴²:

Moles of LiAlH ₄ used for the reduction of different carbonyl-compounds:	
Ketone, Aldehyde:	0,25 mol LiAlH ₄
Ester, Acid Chloride	0,5 mol LiAlH ₄
Carboxylic acid	0,75 mol LiAlH ₄
Nitrile	0,5 mol LiAlH ₄

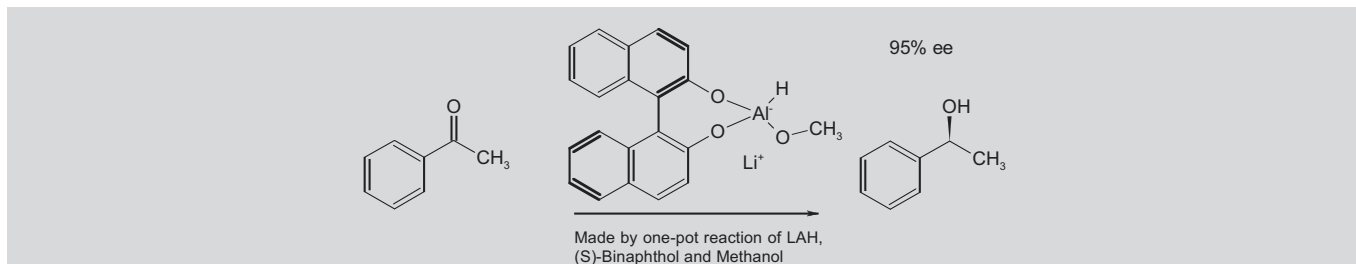
A different mechanism applies for the reduction of sterically hindered iodides. This reaction proceeds via a SET-step involving radical intermediates³⁹.

⁴¹ S. Krishnamurthy, H.C. Brown, J. Org. Chem. 41 (1976) 3064.

⁴² Organikum, 21st ed. Wiley VCh, Weinheim p. 568ff.



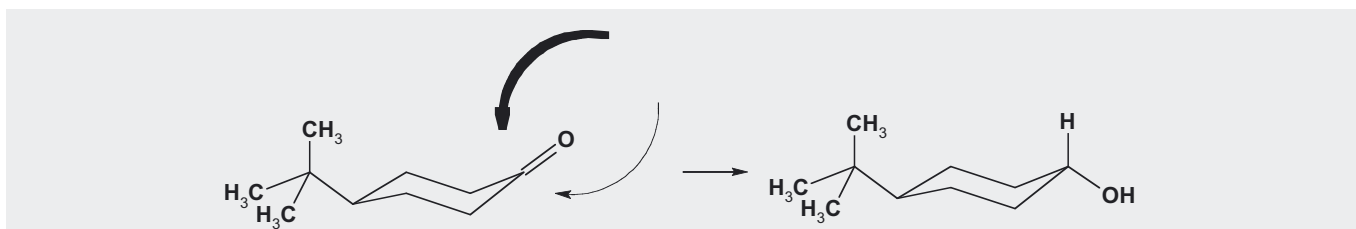
LAH does not reduce isolated double bonds of olefins, but in some cases the double bond of α,β -unsaturated carbonyl-compounds is reduced together with the C=O-bond⁴³. But in general α,β -unsaturated carbonyl-compounds are reduced preferably at the C=O bond, leading to allylic alcohols⁴⁴ and not in a 1,4-manner.



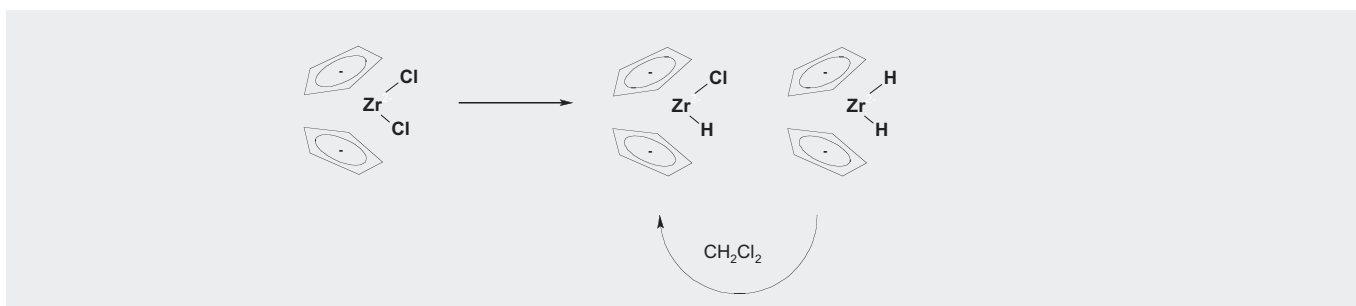
Enantioselective reductions of prochiral ketones are possible with the Noyori-reagent^{45,46}, a mixture of lithium aluminium hydride, a chiral, non-racemic bi-naphthol and a alcohol.

Products from Acros Organics	
(R)-(+)-1,1'-Bi-2-naphthol 99%	22430
(S)-(-)-1,1'-Bi-2-naphthol 99%	22431
1,1'-Bi-2-naphthol 99%	14735

The reduction of 4-tert-butylcyclohexanone with LAH and other sterically not demanding hydride reducing agent proceed preferably from the axial direction⁴⁷.



LAH has been used for the reduction of metalorganic substrates like zirconocene dichloride to chloro bis(cyclopentadienyl) zirconium hydride ("Schwarz' reagent")⁴⁸.



⁴³ Olefinic reduction of α,β -unsaturated carbonyl-compounds by raney-nickel catalyzed hydrosilylation: S.O. Kim, S. Rhee, S.H. Lee, Bull. Korean. Chem. Soc. 20 (1999) 773.

⁴⁴ A. Loupy, J. Seyden-Penne, Tetrahedron 36 (1980) 1937; L.A. Paquette, R.J. Ross, J.P. Springer J. Am. Chem. Soc. 110 (1988) 6192.

⁴⁵ R. Noyori, J. Am. Chem. Soc. 101 (1979) 3129; R. Noyori, Pure Appl. Chem. 53 (1981) 2315.

⁴⁶ R. Noyori, I.Tomino, Y.Tanimoto, M. Nishizawa, J. Am. Chem. Soc. 106 (1984) 6709.

⁴⁷ P.T. Lansbury, R.E. MacLeay, J. Org. Chem. 28 (1963) 1940; S. Winstein, J. Sonnenberg, J. Am. Chem. Soc. 83 (1961) 3235; E.L. Eliel, R.S. Ro, J. Am. Chem. Soc. 79 (1957) 5992; L.A. Paquette, T.L. Underiner, J.C. Gallucci; J. Org. Chem. 57 (1992) 86.

⁴⁸ S.L. Buchwald, S.J. LaMaire, R.B. Nielsen, B.T. Watson, S.M. King, Organic Syntheses, Coll. Vol. 9, 162.



Over-reduced dihydride can be converted to Schwarz reagent by treatment with dichloromethane.

Lithium aluminium deuteride is used for the synthesis of deuterium-labeled compounds from carbonyl-compounds or alkyl halides^{49,50}.

Acros Organics offers several convenient forms of Lithium aluminium hydride either as powder or in solution:

Products from Acros Organics	
Lithium aluminium hydride 95%, powder	19032
Lithium aluminium hydride 95%, pellets	30453
Lithium aluminium hydride 95%, in resealable tin cans	33210
Lithium aluminium hydride, 4.0M solution in diethyl ether	19951
Lithium aluminium hydride, 1,0M solution in THF	19949
Lithium aluminium hydride, 2.4M solution in THF	37732
Lithium aluminium hydride, 15% solution in toluene/THF	38557
Lithium aluminium deuteride 98 atom% D, for NMR	18567

Sodium aluminium hydride is somewhat less reactive and more selective towards the reduction of carboxylic acids, acid chlorides⁵¹, anhydrides and epoxides compared with Lithium aluminium hydride²⁷. SAH has interestingly a complementary reaction rates to certain functional groups as LAH⁵². Nitro-compounds and aromatic isocyanates are reduced faster by SAH, while epoxides are reduced faster with LAH. The lower cost and ease of handling makes SAH a valuable alternative to LAH. SAH is good soluble in ethers like THF (solubility 13-14 wt%) or 1,2-dimethoxyethane. Sodium aluminium hydride has been used for the reduction of N,N-Dimethylamides to aldehydes in THF at 0°C⁵³.

Sodium aluminium hydride has recently received a lot of attention as a possible candidate for hydrogen storage in fuel-cells^{54,55,56}.

Products from Acros Organics	
Sodium aluminium hydride 93%	38011

⁴⁹ M.A. McKinney, S. Nagarjan, J. Org. Chem. 44 (1979) 2233.

⁵⁰ J.E. Baldwin, R.H. Greeley, J. Am. Chem. Soc. 87 (1965) 4514.

⁵¹ J.S. Cha, J.H. Chun, Bull. Korean. Chem. Soc. 21 (2000) 375.

⁵² J.S. Cha, H.C. Brown, The New Journal for Organic Synthesis, 26 (1994) 459.

⁵³ J.S. Cha, H.C. Brown, J. Org. Chem 58 (1993) 4727.

⁵⁴ J. Iñiguez, T. Yildirim, T.J. Udovic, M. Sulic, C.M. Jensen, Phys. Rev.B 70, (2004) 060101-1.

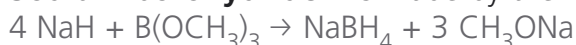
⁵⁵ B. Bogdanovic, J. von Colbe de Bellostá, A. Pommerin, M. Felderhoff, F. Schüth, J. Alloys, Compounds 370, 104-109 (2004).

⁵⁶ B. Bogdanovic, M. Felderhoff, S. Kaskel, A. Pommerin, K. Schlichte, F. Schüth, Adv. Mater. 15, 1012-1015 (2003).



3.3.2. Sodium borohydride and Sodium borodeuteride

Sodium borohydride⁵⁷ is made by the reaction of sodium hydride with borates^{29,58}.



It is usually a white to gray-white powder. It is soluble in water although it decomposes quickly under neutral or acidic conditions; alkaline aqueous solutions or solutions in other protic solvents are relatively stable.

Water and alcohols are therefore the most common solvents for reactions with sodium borohydride, but also ethers like diethyleneglycol dimethylether are used where aprotic conditions are necessary. A notable disadvantage of the reagent is the poor solubility in the common solvents like THF and diethyl ether.

The solubility in different solvents^{59,60} is shown in the following table:

Water	55 g *
Methanol	16,4 g *
Ethanol	4 g *
2-Propanol	0,37 g
THF	0,1 g
Diethylether	slightly soluble
1,2-Dimethoxy ethane	2 g
Diethylene glycol dimethyl ether	6 g
Triethylene glycol dimethyl ether	12 g
Tetraethylene glycol dimethyl ether	15 g
N,N-Dimethylformamide	18 g **
Dimethylsulfoxide	5,8 g *
Solubility per 100 g or ml solvent	
* decomposes in neutral or acidic conditions, relatively stable under alkaline conditions	
** CAUTION: can react violently with this solvent at elevated temperatures	

Boron is less electropositive than aluminium and sodium is a weaker Lewis acid than lithium. This results in a much lower reactivity of sodium borohydride compared with lithium aluminium hydride.

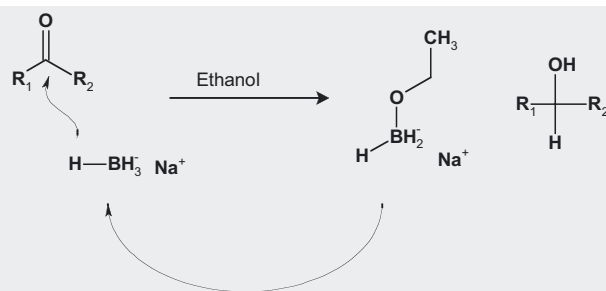
Sodium borohydride in a protic solvent like methanol will react with the solvent and lead to a methoxyborohydride, which is a stronger reductant than neat sodium borohydride itself. The increase in reducing strength is due to the electron donation of the alkoxy-group.

⁵⁷ H.I. Schlesinger, H.C. Brown, H.R. Hoekstra, L.R. Rapp, J. Am. Chem. Soc., 75 (1953) 199.

⁵⁸ Hollemann Wiberg, Lehrbuch der Anorganischen Chemie, de Gruyter, Berlin 1985.

⁵⁹ Source: Productinformation: Glymes from Clariant GmbH.

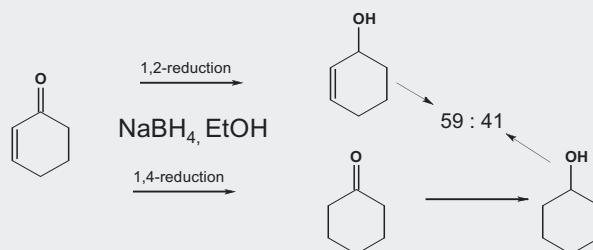
⁶⁰ Source: Productinformation from Finnish Chemicals Oy.



Sodium borohydride in a protic solvent is a mild and selective reducing reagent⁶¹ for **aldehydes** and **ketones** while other functional groups like esters and lactones, epoxides, carboxylic acids and carboxylates etc. remain mostly unchanged. Carboxylic acid halides are usually reduced to the corresponding alcohol⁶².

All four hydrogen atoms can be used for reduction, so one mole of borohydride can reduce four moles of aldehydes or ketone.

The hydride ion in sodium borohydride is a weaker nucleophile compared with LAH, thus the 1,4-addition to α,β -unsaturated carbonyl compounds becomes equally important than the 1,2-addition, which leads usually to a mixture of 1,2- and 1,4-product²⁷. The selectivity is strongly influenced by the solvents and substrates⁶³ but generally not satisfying.



In the presence of Cerium salts the 1,2-addition is strongly preferred^{64,65} ("Luche reduction"). The Luche reduction is a very popular method for the synthesis of allylic alcohols (see examples A⁶⁶, B⁶⁷, C⁶⁸).

⁶¹ L. Zhenjiang, Synlett, 1 (2005) 182.

⁶² R.C. Larock Comprehensive Organics Transformations, Second Edition, Wiley VCh, New York, 1999 p 1114 ff.

⁶³ C.F. Nutaitis, J.E. Bernardo, J. Org. Chem. 54 (1989) 5629.

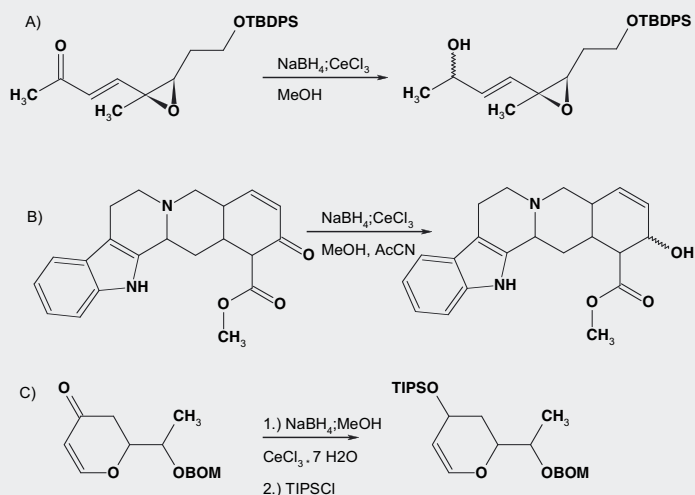
⁶⁴ J.-L. Luche, J. Am. Chem. Soc., 100 (1978) 2226; D. Turner, P. Vogel, Synlett, (1998), 304.

⁶⁵ A.L. Gemal, J.-L. Luche, J. Am. Chem. Soc. 103 (1981), 5454.

⁶⁶ W. Picoul, O. Bedel, A. Haudrechy, Y. Langlois, Pure Appl. Chem., 75 (2003) 235.

⁶⁷ F. Binns, T.R. Brown, B.E.N. Dauda, Tetrahedron Lett. 41 (2000) 5631.

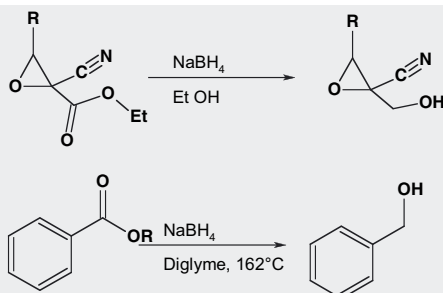
⁶⁸ D. Meng, P. Bertinato, A. Balong, D.-S. Su, T. Kamencka, E.K. Sorensen, S.J. Danishefsky, J. Am. Chem. Soc. 119 (1997) 10073.



The addition of 1-3 equivalents glacial acetic acid to sodium borohydride in THF leads to the formation of sodium mono-, di- or triacetoxyborohydride (vide infra) in the reaction mixture, which act as much milder and more selective reducing agents and shift the selectivity towards the 1,2-reduction⁶³.

The relative reactivity of carbonyl functionalities towards reduction with sodium borohydride follows the order²⁷:

Aldehydes > α,β -unsaturated aldehydes > ketones > α,β -unsaturated ketones



The reduction of carboxylic esters is normally slow and other reagents like lithium borohydride or lithium aluminium hydride are more suitable for this reaction, but the selectivity of the reagent is sometimes advantageous as demonstrated in the following reduction where only the ester is reduced and the cyano- and epoxy (!)-group remains unaffected⁶⁹:

In aprotic solvents like diglyme sodium borohydride can reduce esters only at high temperatures⁷⁰.

In aqueous solvents (under S_N1 conditions) sodium borohydride reacts readily with secondary and tertiary halides and tosylates⁷¹, while in anhydrous diglyme under S_N2 -conditions the reaction is generally slower and primary halides are faster reduced than secondary^{36,72}. Many other examples for reductions of halides and other leaving groups in polar aprotic solvents have been reported⁷³.

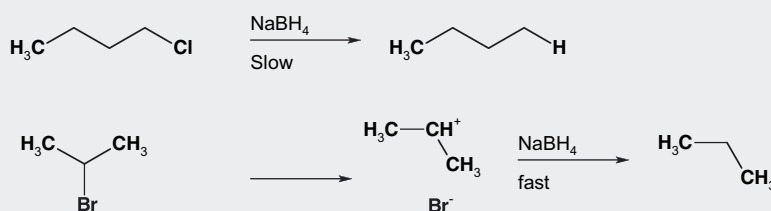
⁶⁹ J. Mauger, A. Robert, Chem. Comm. 1986, 395; J. Mauger, A. Robert, Tetrahedron 1988, 44, 2493.

⁷⁰ H.J. Zhu, C.U. Pittman, Jr., Synthetic Communications, 33, (2003) 1733.

⁷¹ H.M. Bell, H.C. Brown, J. Am. Chem. Soc. 88 (1966) 1473.

⁷² H.M. Bell, C.W. Vanderslice, A. Spehar, J. Org. Chem. 34 (1969) 3923.

⁷³ R.O. Hutchins, D. Kandasamy, F. Dux III, C.A. Mayanoff, D. Rotstein, B. Goldsmith, W. Burgoyne, F. Cistone, J. Dalessandro, D. Puglis J. Org. Chem. 43 (1978) 2259.



The reactivity of sodium borohydride can be drastically increased by the addition of Lewis acids^{74,75,76} in different ways:

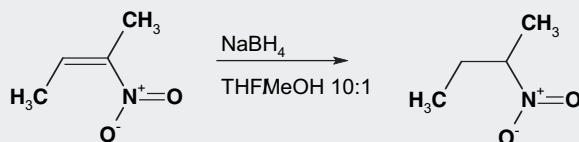
- 1.) Lewis acids like boron trifluoride⁷⁷, aluminium chloride, iodine or chlorotrimethylsilane⁷⁸ react with sodium borohydride to yield borane⁷⁹ complexes, which is a stronger reducing agent²⁷.
- 2.) Carbonyl compounds are activated for the nucleophilic attack by Lewis acid.

The latter point is particularly interesting for the reduction of C-N-double bonds as in imines, oximes or iminium salts. Their reactivity is normally small, but a complexation with Bronstedt- or Lewis acids like titanium tetrachloride or nickel(II) chloride increases their reactivity drastically, although sodium cyanoborohydride is still the reagent of choice for the reduction of C-N-double bonds (*vide infra*).

Many additives have been used for the activation of sodium borohydride⁸⁰:

Cerium(III) chloride⁸¹, calcium chloride⁷⁴, zinc chloride⁸², copper(II) sulfate, iodine, borane dimethylsulfide complex

The activation of borohydride with (Lewis-) acids makes many more functional groups reducible^{80,60}.



Other reactions of sodium borohydride are the selective reduction of nitroalkenes to nitroalkanes⁸³ and the selective reduction of acid chlorides to aldehydes in DMF at 0°C the presence of pyridine, which act as a borane scavenger⁸⁴ to avoid over reduction to the alcohol.

⁷⁴ H.C. Brown, S. Narasimhan, Y.M. Choi, J. Org. Chem. 47 (1982) 4702.

⁷⁵ H.C. Brown, B.C. Subba Rao, J. Am. Chem. Soc. 78 (1956) 2582.

⁷⁶ S. Bhattacharyya, Synth. Comm. 25 (1995) 2061.

⁷⁷ S.-D. Cho, Y.-D. Park, J.-J. Kim, J.R. Falck, Y.-J. Yoon, Bull. Korean. Chem. Soc. 25 (2005) 407.

⁷⁸ A. Giannis, K. Sandhoff, Angew. Chem. Int. Ed. Engl. 28,(1989) 218.

⁷⁹ N.M. Yoon, C.S. Pak, H.C. Brown, S. Krishnamurthy, T.P. Stocky, J. Org. Chem. 38 (1973) 2786.

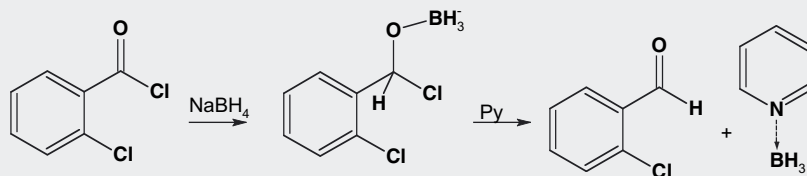
⁸⁰ M. Periasamy, M. Thirumalaikumar, J. Organometal. Chem. 609 (2000) 137.

⁸¹ D.E. Ward, C.K. Rhee, Can. J. Chem. 67 (1989) 1206.

⁸² T. Yamakawa, M. Masaki, H. Nohira, Bull. Chem. Soc. Jap. 64 (1991) 2730.

⁸³ R.S. Varma, G.W. Kabalka, Synth. Comm. 15(2), (1985) 151-155

⁸⁴ J.H. Babler Synth. Comm. 12, (1982) 839-846.



The reduction of prochiral ketones with sodium borohydride in the presence of chiral cobalt-complexes⁸⁵ and other chiral ligands⁸⁶ has led to chiral alcohols in high enantiomeric excess

Products from Acros Organics	
Sodium borodeuteride 98 atom% D, for NMR	19495
Sodium borohydride, 12% solution in 40% aq. sodium hydroxide solution	38993
Sodium borohydride 98%, granules, ca 3 mm	41947
Sodium borohydride 98%, (12-13 mm), pellets, 7/16"	20148
Sodium borohydride, 0.5 M solution in diglyme	19113
Sodium borohydride 99%, powder	20005
Sodium borohydride 98+%, powder	18930

3.4 Tuning of the reactivity by different substituents: Derivatives with different sterical and electronical properties

Sodium borohydride and lithium aluminium hydride mark the extremes in the scale of reactivity towards a variety of functional groups.

In general the reactivity of a hydride reducing agent is strongly influenced by the following factors:

- The bulkiness of the reagent
- The inductive effect of the substituents
- The Lewis acidity of the counterion
- The solubility in different solvents

Many derivatives with different sterically and electronical properties are used for special applications.

The following examples will provide a brief overview on the most important reagents:

⁸⁵ T. Nagata, K. Yorozu, T. Yamada, T. Mukaiyama, *Angew. Chem.* 107 (1995) 2309.

⁸⁶ Z. Zhenghong, T. Yilong, W. Lixin, Z. Guofeng, Z. Qilin, T. Chuchi, *Synthesis* (2004) 217.



3.5 Modified borohydrides

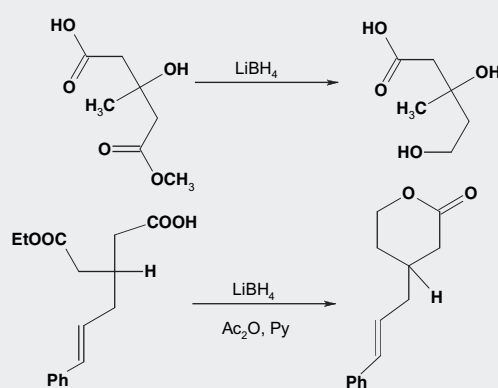
3.5.1. Lithium borohydride

Lithium borohydride is made from sodium borohydride and lithium chloride or bromide⁷⁴. It is a white crystalline powder which melts with decomposition at 280°C. In contrast to sodium borohydride it is easily soluble in diethyl ether and other ethereal solvents⁷⁴, in amines and reacts quickly with water but only slowly with cold absolute alcohols.

Solubility of Lithium borohydride in different solvents	
Diethylether	3 g / 100 ml
THF	25 g / 100 ml
Diglyme	9 g / 100 ml
Methanol	1,6 g / 100 ml*
Ethanol	2,3 g / 100 ml*
2-Propanol	3 g / 100 ml *
* reacts with solvent	

It is less reactive than lithium aluminium hydride but far more reactive than sodium borohydride. Acid chlorides, esters, aldehydes, ketones and epoxides are reduced to the alcohols whereas carboxylic acids, nitriles and nitro compounds are not reduced.

Aldehydes and ketones are easily reduced in THF solution at low temperature⁸⁷, lactones and esters are only reduced at higher temperatures. Lithium borohydride is a valuable reduction reagent when a selectivity between different carbonyl functionalities is important^{88,89}.



The reactivity of lithium borohydride is influenced strongly by the solvent⁷⁴:
Diethyl ether > THF ~ Diglyme > 2-Propanol

⁸⁷ R.F. Nystrom, S.W. Chaikin, W.G. Brown, J. Am. Chem. Soc. 71 (1949) 3245.

⁸⁸ F.-C. Huang, L.F. Lee, R.S.D. Mittal, P.R. Ravikumar, J.A. Chan, C.J. Sih, J. Am. Chem. Soc. 97 (1975) 4144.

⁸⁹ S. Kobayashi, M. Nakada, M. Ohno, Pure. Applied. Chem. 64 (1992) 1121.



Also the reducing capability of lithium borohydride can be increased by the addition of one or more equivalents of methanol to the ethereal solution^{90,91}.

Halides or tosylates are not reduced by lithium borohydride but N,N-disubstituted amides are slowly reduced to aldehydes.

The Acros Organics lithium borohydride is available as powder or solution in THF.

Products from Acros Organics	
Lithium borohydride, 2M solution in tetrahydrofuran	21293
Lithium borohydride 95%,	20681

3.5.2. Potassium borohydride

The reactivity of potassium borohydride is comparable to sodium borohydride, but it is less hygroscopic, somewhat more stable and has a different solubility in several solvents^{60,92}

Solubility in 100 g solvent	
Water	19,3 g
Dimethylformamide	15 g
Dimethylsulfoxide	7,6 g
Methanol	0,7 g

Acros Organics potassium borohydride is available as solid.

Products from Acros Organics	
Potassium borohydride 98%,	19665

3.5.3. Tetraalkylammonium- and tetraalkylphosphonium borohydrides^{93,94,95,96}

In general tetraalkylammonium borohydrides^{97,98} can be compared with the alkali-borohydrides.

Since the short-chain tetramethylammonium derivatives have a rather poor solubility in different solvents and the long chain derivatives show a somewhat weak reactivity⁹⁹ these compounds have only found little attention as reagents.

⁹⁰ K. Soai, A. Ookawa, J. Org. Chem. 51 (1984) 4000.

⁹¹ K. Soai, H. Oyamada, M. Takase, A. Ookawa. Bull. Chem. Soc. Jpn. 57 (1984) 1948.

⁹² Chemetall GmbH Product Information.

⁹³ K.S. Ravikumar et al J. Org. Chem. 58, 5981, (1993); K.S. Ravikumar et al Tet. Lett. 34, 171, (1993).

⁹⁴ Fieser & Fieser, Reagents for Organic Synthesis Vol VI, Wiley, New York, 1977.

⁹⁵ H.J. Zhu, C.U. Pittman, Synth. Comm. 33 (2003) 1733.

⁹⁶ A. Datta, M. Hepperle, G.I. Georg, J. Org. Chem. 50 (1995) 761.

⁹⁷ M.D. Banus, R.W. Bragdon, T.R.P. Gibb, J. Am. Chem. Soc. 74 (1952) 2346.

⁹⁸ D.J. Raber, W.C. Guida, J. Org. Chem. 41 (1976) 690.

⁹⁹ E.A. Sullivan, A.A. Hinckley, J. Org. Chem. 27 (1962) 3731.



Tetrabutylammonium borohydride on the other hand has a good solubility in dichloromethane¹⁰⁰ and can be used as a mild and selective reducing agent for acid chlorides, ketones and aldehydes. Also nitriles and amides have been reduced successfully with tetrabutylammonium borohydride in dichloromethane¹⁰¹.

Tetrabutylammonium borohydride has been used for the reduction of acylferrocenes to alkylferrocenes in the presence of zinc chloride¹⁰².

The following Acros Organics tetraalkylammonium- and tetraalkylphosphonium borohydrides are available.

Products from Acros Organics	
Benzyltriphenylphosphonium borohydride 95%	37637
Benzyltriethylammonium borohydride 96%	30247
Tetrabutylammonium borohydride 98%	21290

3.5.4. Calcium borohydride

Calcium borohydride is not stable enough to be commercially available but it can be prepared by the reaction of sodium borohydride with calcium chloride.

It is a facile reagent for the reduction of carboxylic esters to alcohols^{103,104}.

3.5.5. Sodium cyanoborohydride¹⁰⁵

Sodium cyanoborohydride is made by the reaction of hydrogencyanide with sodium borohydride.

It is a very **toxic**, white, hygroscopic powder with a melting point of ca. 240-242°C.

The solubility of sodium cyanoborohydride¹⁰⁶ in 100 g of different solvent is shown in the following table:

THF	37 g
Water	212 g
Diethylether	insoluble
Methanol	very soluble
Benzene	insoluble
Hexane	insoluble
Diethylene glycol dimethyl ether	18 g

¹⁰⁰ A. Brandström, U. Junggren, B. Lamm, *Tetrahedron Lett.* (1972) 3173.

¹⁰¹ T. Wakamatsu, H. Inaki, A. Ogawa, M. Watanabe, Y. Ban, *Heterocycles* 14 (1980) 1437.

¹⁰² S. Bhattacharyya, *Synlett* 1998, 837.

¹⁰³ S. Narasimhan, K. Ganeshwar Prasad, S. Madhavan, *Synth. Commun.* 25 (1995) 1689.

¹⁰⁴ C.T. Evans, S.M. Roberts, K.A. Shoberu, A.G. Sutherland, *J. Chem. Soc., Perkin Trans. 1*, 1992, 589.

¹⁰⁵ C.F. Lane, *Synthesis* 1975, 135.

¹⁰⁶ R.C. Wade, E.A. Sullivan, J.R. Berscheid, K.F. Purcell, *Inorg. Chem.* 9 (1970) 2146.



The reagent is surprisingly stable in acidic solvents down to pH 3¹⁰⁷, only in very acidic media like 12 N hydrochloric acid, rapid hydrolysis occurs¹⁰⁸:



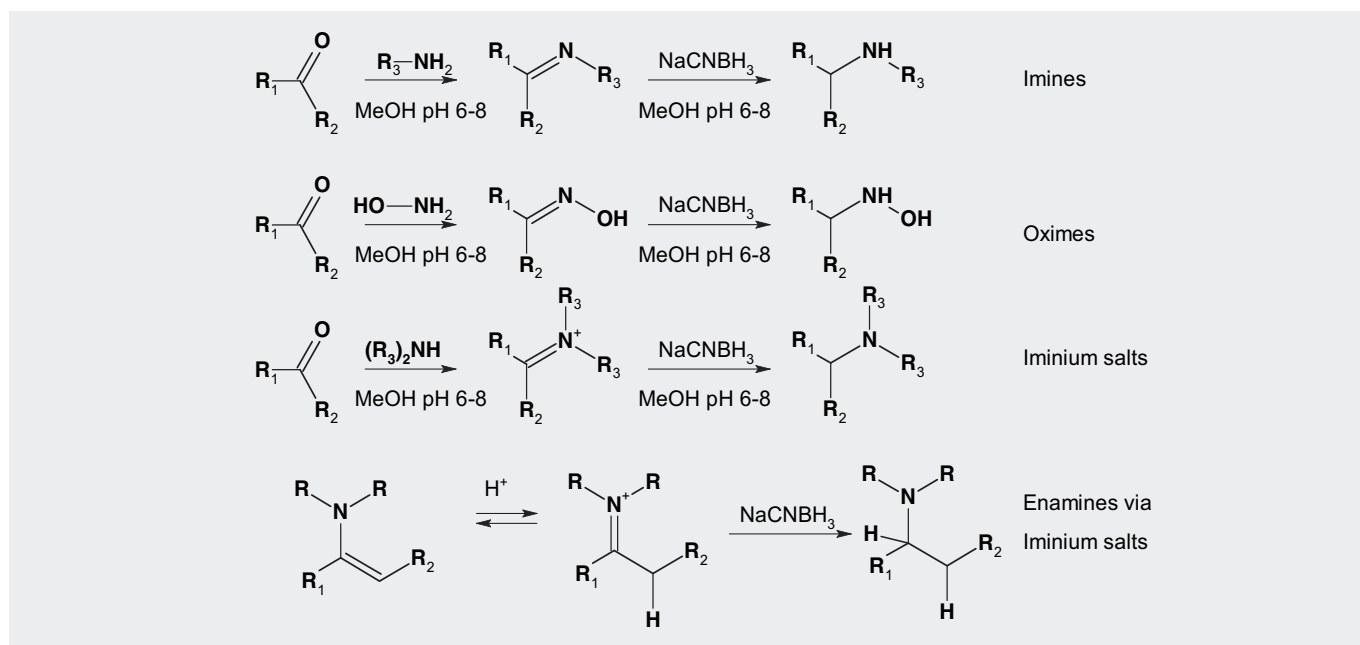
The cyanide-ion is a strong electron withdrawing group which makes the hydride ions in the cyanoborohydride to weaker nucleophiles compared with sodium borohydride¹⁰⁹. The reductive power in cyanoborohydride is therefore significantly smaller.

This and the stability in acidic solutions is responsible for the high selectivity in reduction reactions and makes sodium cyanoborohydride unique in the group of borohydrides and aluminiumhydrides:

- Sodium cyanoborohydride reduces C=N-bonds faster than C=O bonds
- C=O-bonds of aldehydes and ketones are only reduced at low pH, under neutral conditions there is virtually no reduction of these functional groups

These two properties open the door for the most valuable applications of cyanoborohydride:

- the reductive amination of carbonyl compounds or vice versa
- the reductive alkylation of amines
- the reduction of enamines, oximes etc.



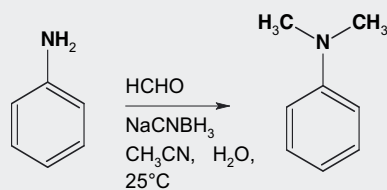
¹⁰⁷ R.F. Borch, H.D. Durst, J. Am. Chem. Soc. 91 (1969) 3996.

¹⁰⁸ J.R. Berschied, K.F. Purcell, Inorg. Chem. 9 (1970) 624.

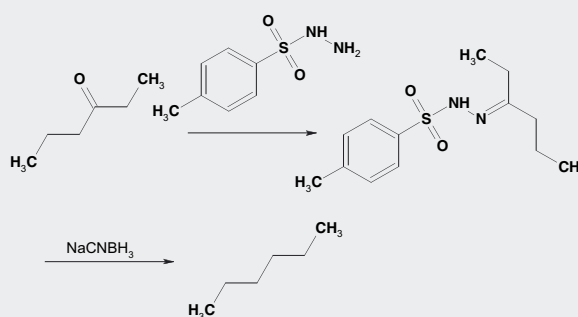
¹⁰⁹ Organikum, 21st ed. Wiley VCh, Weinheim 2001.



The use of formaldehyde as carbonyl component opens the way to the reductive methylation of amines¹¹⁰ via the imine:



Other reactions with cyanoborohydride include the reduction of aldehydes and ketones to hydrocarbons via the p-tosylhydrazones^{111,112}.



Products from Acros Organics

4-Methylbenzenesulfonylhydrazide 97%	15786
Sodium cyanoborohydride 95%	16855
Silicagel, functionalized, (trimethylammonium)propyl cyanoborohydride, ca. 1 mmol/g, part. size: 120-200micron	37154

¹¹⁰ R.F. Borch, A.I. Hassid, J. Org. Chem. 37, 1673, 1972.

¹¹¹ R. O. Hutchins, M. Kacher, and L. Rua, J. Org. Chem. 40 (1975) 923; R.O. Hutchins, C.A. Milewski, B. Maryanoff, J. Am. Chem. Soc. 95 (1973) 3662.

¹¹² Organic Syntheses, Coll. Vol. 6, p.293; Vol. 59, p.42.



3.5.6. Sodium triacetoxyborohydride

Sodium triacetoxyborohydride is available as white powder with a melting point of ca. 116-120°C, but can also be made easily *in situ* from sodium borohydride and 3 equivalents of acetic acid¹¹³.

Compared with sodium borohydride the boron-hydrogen bond is stabilized by sterical and electron-withdrawing effects of the acetoxy-groups, making sodium triacetoxyborohydride an even milder reducing agent with weak hydride donor capabilities.

The reaction of sodium borohydride with one equivalent carboxylic acid leads to the mono-acyloxyborohydride, which is generally more reactive (or better less deactivated) than sodium triacetoxyborohydride. The mono-acyloxyborohydride can reduce amides and lactams and nitriles to amines^{114,115} which is not possible with the triacetoxyborohydride.

Di- and tri-arylcarbinols and diaryl and ketones can be reduced to hydrocarbons by a reagent made from sodium borohydride with one equivalent of trifluoroacetic acid.

Sodium triacetoxyborohydride is not very good soluble in organic solvents¹¹⁶:

Hydrocarbons	almost insoluble
Diethyl ether	almost insoluble
THF	<2 wt%, 20°C
DME	<5 wt%, 20°C

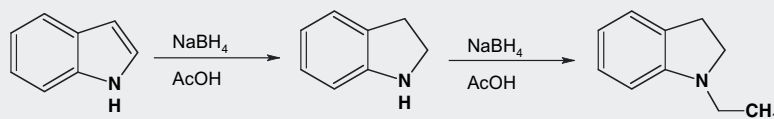
It is mostly employed as a slurry or suspension in THF, dichloromethane or benzene (with or without a addition of anhydrous acetic acid)¹¹⁷.

Sodium triacetoxyborohydride has two major applications:

- the reduction of aldehydes in the presence of ketones^{118,119}
- the reductive amination of aldehydes and ketones¹¹⁷.

Also other reactions can be performed with this reagent:

- reduction and subsequent N-alkylation of indoles and quinolines



¹¹³ G.W. Gribble, Chem. Soc. Rev. 27 (1998) 395.

¹¹⁴ N. Umino, T. Iwakuma, M. Itoh, Tetrahedron Lett (1976) 763.

¹¹⁵ N. Umino, T. Iwakuma, M. Itoh, Tetrahedron Lett (1976) 2875.

¹¹⁶ Chemetall GmbH, product information.

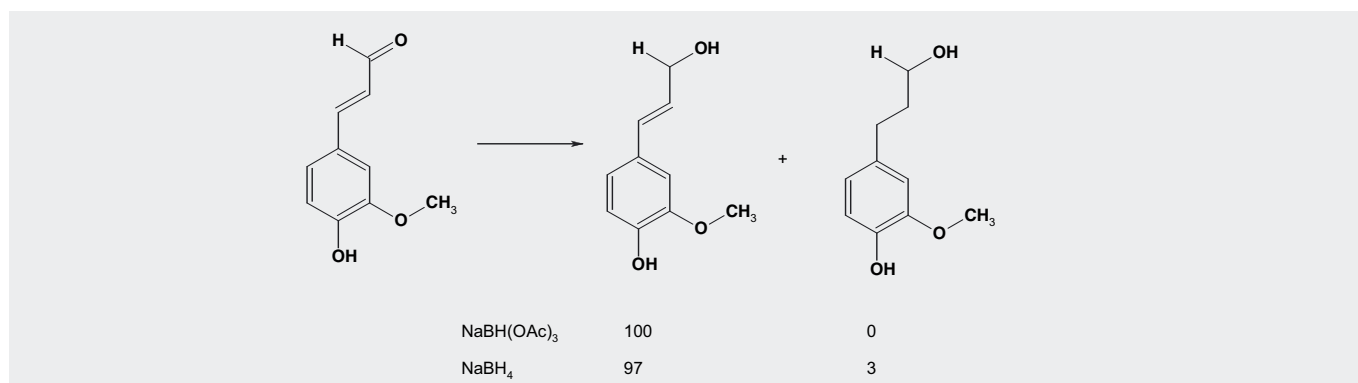
¹¹⁷ A.F. Abdel-Magid, K.G. Carson, B.D. Harris, C.A. Maryanoff, R.D. Shah, J. Org. Chem. 61 (1996) 3849.

¹¹⁸ G.W. Gribble, D.C. Ferguson, J. Chem. Soc. Chem. Comm. (1975) 535.

¹¹⁹ C.F. Nutaitis, G.W. Gribble, Tetrahedron Lett. 24 (1983) 4287.



- highly selective 1,2-reduction rather than 1,4-reduction of α,β -unsaturated aldehydes^{120,63}



Products from Acros Organics

Sodium triacetoxyborohydride 97%

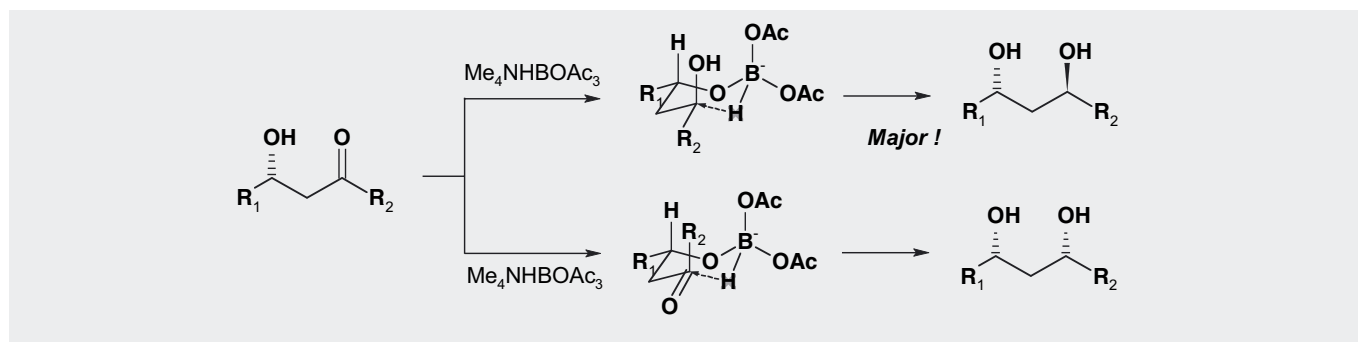
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3.5.7. Tetramethylammonium triacetoxyborohydride¹²¹ (NEW: AO 39285)

TABH is made by the reaction of Tetramethylammonium hydroxide (AO 36632 as 40% solution in methanol) with Sodium borohydride followed by the reaction with three equivalents of acetic acid.

It is a stable, but moisture sensitive solid, which is soluble in many organic solvents including methylenechloride, chloroform or acetonitrile.

The major synthetic application of TABH is the *anti*-selective reduction of β -hydroxyketones as illustrated in the following scheme:



The diastereoselective outcome of the reduction of β -hydroxyoximino ethers with TABH is dependent on the configuration at the imino-group¹²².

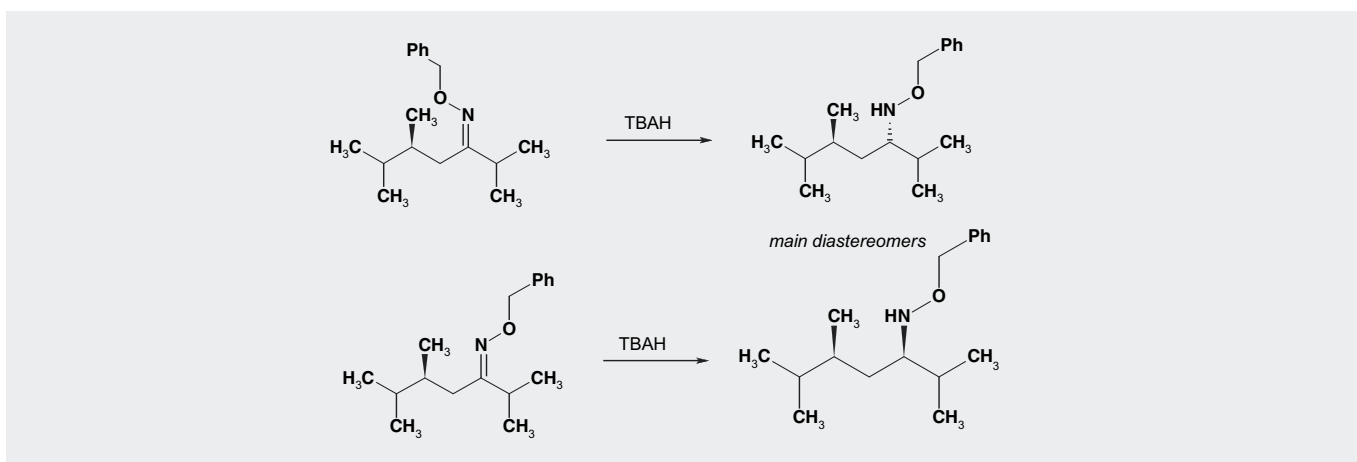
¹²⁰ F. Lu, J. Ralph, J. Agric. Food. Chem. 46 (1998) 1794.

¹²¹ D.A. Evans, K.T. Chapman, E.M. Carreira, J. Am. Chem. Soc. 110 (1988) 3560.

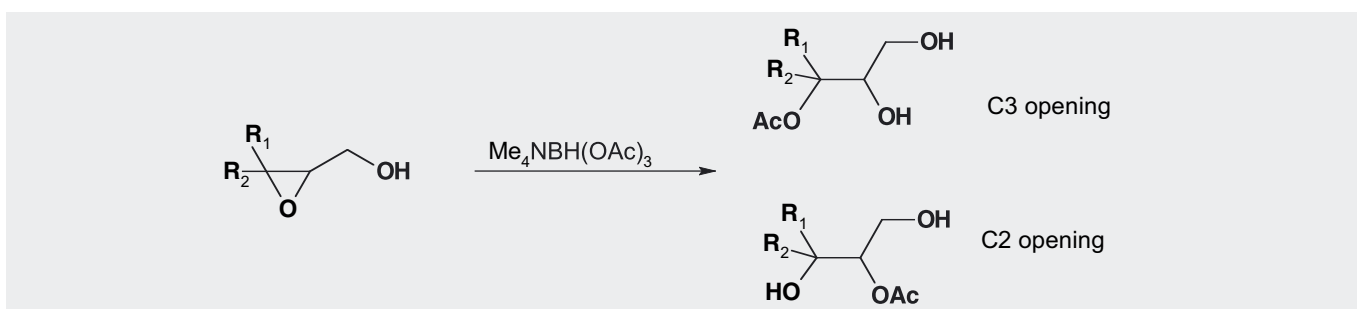
¹²² D.R. Williams, M.H. Osterhout, J. Am. Chem. Soc. 114 (1992) 8750.



Z-configured oximino ethers are reduced mainly to the *anti*-product, while E-configured oximino ethers are highly specific reduced to the *syn*-products:



TBAH has also been used for the regioselective ring-opening of 2,3-epoxyalcohols¹²³



The reaction leads preferably to the "C3 opening" products.



3.6 Alkoholate modified aluminium hydrides

In contrast to borohydrides, where the reducing capabilities are increased by alkoxy substituents^{124,125} aluminium hydrides are weakened by alkoxy-groups. The following two examples show the attenuation of the reducing power and increasing selectivity.

3.6.1. Lithium triethoxyaluminium hydride^{126,127,128} is made by the reaction of lithiumaluminium hydride with dry ethyl acetate (1.5 eq) or ethanol (3 eq). It is a mild and selective reducing agent for the reduction of nitriles and tertiary amides to aldehydes^{129,130,131,132}.

3.6.2. Lithium tri-tert-butoxyaluminumhydride

Lithium tri-tert-butoxyaluminumhydride is a stable solid, commercially supplied as powder or as solution in THF. The other tri-alkoxy aluminium hydrides are unstable and are made in situ¹³³.

Solubility (at 25°C)
36g/100ml THF
2g/100g Diethyl ether
4g/100 g Dimethoxyethan
41g/100g Diglyme

The reagent is used for the selective reduction of acid chlorides to aldehydes¹³⁴ and for the selective reduction of ketones in the presence of esters¹³⁵. Lithium tri-tert-butoxyaluminumhydride can reduce aldehydes, ketones, acid chlorides and (but much slower) epoxides and esters. Carboxylic acids, amides, nitriles and nitro compounds are not reduced.

Products from Acros Organics	
Lithium tri-tert-butoxyaluminumhydride, 1.1M solution in THF	37758
Lithium tri-tert-butoxyaluminumhydride 93-98%	12516

3.6.3 Sodium bis(2-methoxyethoxy)aluminiumhydride ("SMEAH")

Sodium bis(2-methoxyethoxy)aluminiumhydride is a powerful reducing agent with comparable characteristics to lithiumaluminium hydride. It is easily soluble in aromatic hydrocarbons, diethyl ether, THF and DME and it is insoluble in aliphatic hydrocarbons. It is commercially mostly supplied as a 70% (~3.4 M) solution in toluene.

The good solubility and the non-pyrophoric properties of SMEAH are advantageous compared with LAH.

¹²⁴ H.C. Brown, E.J. Mead, C.J. Shoaf, J. Am. Chem. Soc. 78 (1956) 3613.

¹²⁵ H.C. Brown, E.J. Mead, C.J. Shoaf, J. Am. Chem. Soc. 78 (1956) 3616.

¹²⁶ H.C. Brown, A. Tsukamoto, J. Am. Chem. Soc. 86 (1964) 1089.

¹²⁷ A.G. Myers, B.H. Young, H. Chen, Organic syntheses, Coll. Vol. 10, 509.

¹²⁸ A.G. Myers, B.H. Yang, H. Chen, L. McKinsty, D.J. Kopecky, J.L. Gleason, J. Am. Chem. Soc. 119 (1997) 6496.

¹²⁹ H.C. Brown, C.J. Shoaf, J. Am. Chem. Soc. 86 (1964) 1079.

¹³⁰ H.C. Brown, C.P. Garg, J. Am. Chem. Soc. 86 (1964) 1085.

¹³¹ H.C. Brown, S. Krishnamurthy, Tetrahedron 35 (1979) 567.

¹³² dePeretti, T. Strzalko-Bottin, J. Seyden-Penne Bull, Soc. Chim. Fr. 1974, 2925.

¹³³ H.C. Brown, P.M. Weissman, J. Am. Chem. Soc. 87 (1965) 5614.

¹³⁴ J.E. Siggins, A.A. Larsen, J.H. Ackerman, C.D. Carabateas, Organic Syntheses, Coll. Vol. 6, p.529.

¹³⁵ K. Heusler, P. Wieland, Ch. Meystre, Organic Syntheses, Coll. Vol. 5, p.692.



SMEAHA reduces a wide range of functional groups: carboxylic esters, acid chlorides, anhydrides, aldehydes¹³⁶ and ketones are reduced to the alcohols. Carboxylic esters, especially the phenyl and tert. -butylesters are stable towards SMEAH at low temperatures

A major difference in the reactivity to lithiumaluminiumhydride is the reactivity towards nitriles, which are selectively reduced to aldehydes and the reactivity towards aromatic aldehydes which are reduced to the alkane.

Products from Acros Organics

Sodium bis(2-methoxyethoxy)aluminiumhydride, 70 wt% sol. in toluene (ca. 3.5M)

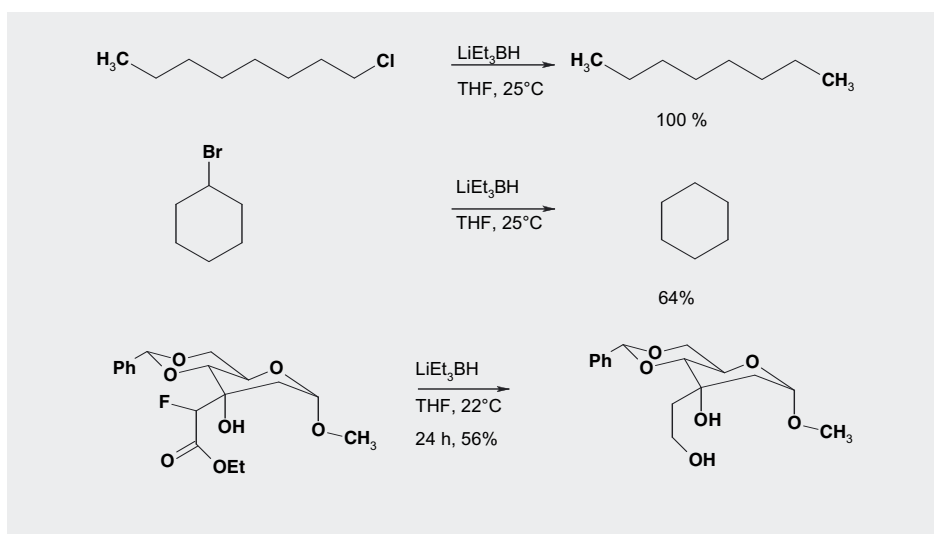
18790

3.7 Alkylsubstituted borohydrides

3.7.1. Triethylborohydrides

Lithium triethylborohydride¹³⁷ is made from lithiumhydride and triethylborane¹³⁸, tert-butyllithium and triethylborane or lithium aluminium hydride and triethylborane¹³⁹ in the presence of triethylenediamine. It is commercially available as solution in THF. Lithium triethylborohydride is an extremely powerful hydride-nucleophile. The relative nucleophilicity of different groups are listed in the following table¹³⁸.

Et ₃ BH	9.400.000
NbuS ⁻	680.000
PhS ⁻	470.000
AlH ₄ ⁻	230.000
Iodide	3.700
Ethanolate	1.000
BH ₄ ⁻	940
Bromide	500
Phenolate	400
Nitrate	100



Lithium triethylborohydride is the reagent of choice for the reduction of alkyl halides. Primary alkyl iodides are reduced most easily¹³⁸, but also fluorides can be reduced to the hydrocarbon¹⁴⁰.

¹³⁶ K. Hagiya, S. Mitsui, H. Taguchi Synthesis 6 (2006) 823.

¹³⁷ H.C. Brown, S.C. Kim, S. Krishnamurthy, J. Org. Chem. 45 (1980) 1.

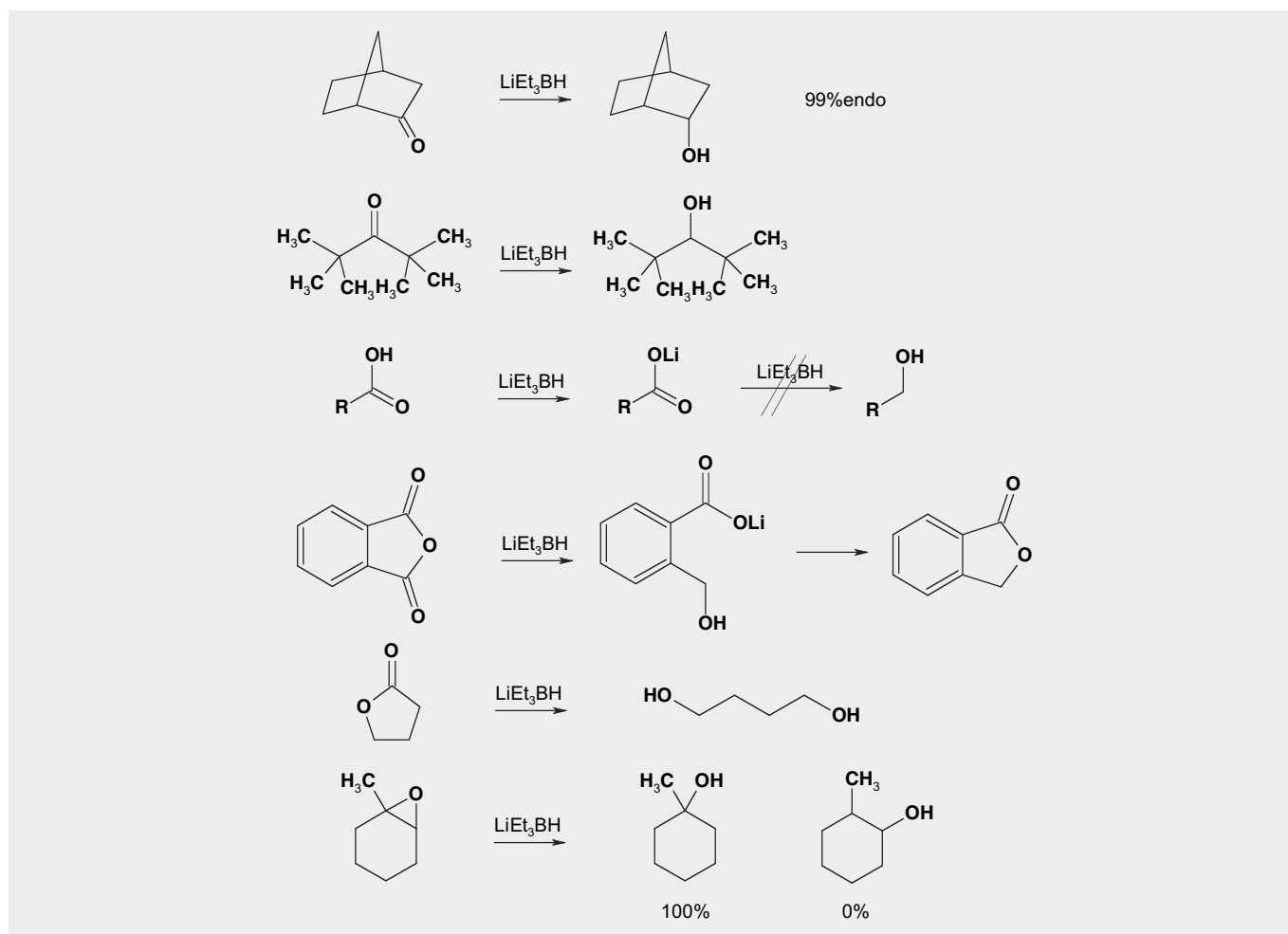
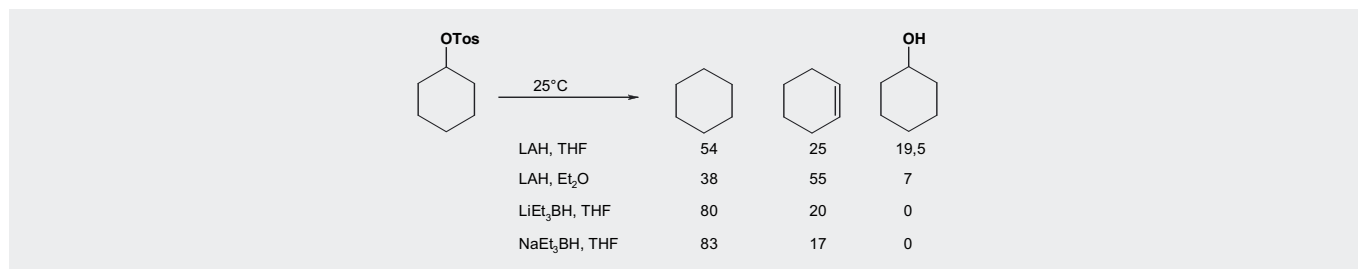
¹³⁸ S. Krishnamurthy, H.C. Brown, J. Org. Chem. 48 (1983) 3085.

¹³⁹ H.C. Brown, G.W. Kramer, J.L. Hubbard, S. Krishnamurthy, J. Organometal. Chem. 188 (1980) 1.

¹⁴⁰ S. Brandäge, O. Dahlmann, J. Ölund, J. Am. Chem. Soc. 103 (1981) 4452.



Alcohols can be reduced via the tosylates⁴¹ or the mesylates.



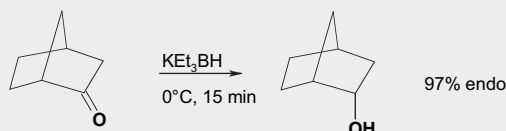
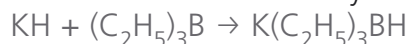
Lithium triethylborohydride is also a good reagent for the reduction of aldehydes and ketones to alcohols, even the very sterically hindered di-tert-butylketone reacts smoothly¹³⁷. Also esters and acid chlorides are reduced to and carboxylic esters are very easily reduced to alcohols. Surprisingly carboxylic acids are resistant towards a reduction with lithium triethylborohydride and consequently anhydrides are also not completely reduced leading to a mixture of carboxylic acid and alcohol or for cyclic anhydrides to lactones as end-products. Epoxides are opened rapidly and quantitatively, yielding the higher substituted "Markovnikov"-product in the case of unsymmetric epoxides¹³⁷. Acetals, ketals and ortho-ester are inert towards Lithium triethylborohydride.

Tertiary amides are reduced to alcohols (and not to amines as with other hydride reducing agents).



Aliphatic nitriles are reduced to primary amines only in low yield, but benzonitrile can be reduced to benzylamine in good yield. Isoquinolines and pyridines are reduced to tetrahydroisoquinolines and to piperidines¹⁴¹ or tetrahydropyridines¹³⁷. Lithium triethylborohydride adds to substituted styrenes in "Markovnikov"-orientation¹⁴².

Potassium triethylborohydride^{143, 144} is commercially available as 1 M solution in THF. It is made by the reaction of sodium hydride with triethylborane in THF:



Potassium triethylborohydride is a strong reducing agent which is somewhat slower than Lithium triethylborohydride. It reduces readily a number of functional groups¹⁴³ like aldehydes, esters, ketones and acid chlorides to alcohols, cyclic anhydrides to lactones, epoxides to the higher substituted alcohol.

Primary bromides are reduced fast to the hydrocarbons, but primary chlorides and secondary bromides react only slowly.

Sodium triethylborohydride is made by the reaction of sodium hydride with triethylborane¹⁴⁵. It has been used for the reductive desulfurisation of thiols and thioketones¹⁴⁶.

Products from Acros Organics

Lithium triethylborohydride, 1M solution in THF	17699
Potassium triethylborohydride, 1 M solution in tetrahydrofuran	20004
Sodium triethylborohydride, 1 M solution in tetrahydrofuran	20003

¹⁴¹ B.E. Blough, F.I. Carroll, Tetrahedron Lett. 34 (1993) 7239.

¹⁴² H.C. Brown, S.C. Kim, J. Org. Chem. 49 (1984) 1064.

¹⁴³ N.M. Yoon, H.S. Yang, Y.S. Hwang Bull. Korean. Chem. Soc. 8 (1987) 285.

¹⁴⁴ N.M. Yoon, H.S. Yang, Y.S. Hwang Bull. Korean. Chem. Soc. 10 (1989) 205.

¹⁴⁵ J.B. Honeycutt jr., J.M. Riddle, J. Am. Chem. Soc. 83 (1961) 369.

¹⁴⁶ H. Alper, S. Ripley, T.L. Prince, J. Org. Chem. 48 (1983) 250.



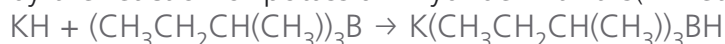
3.7.2. Tri sec-butylborohydrides and trisamylborohydrides

The alkali tri sec-butylborohydrides are soluble in ethereal solvents like ether and THF and they are usually supplied as such solutions.

Lithium tri-sec-butylborohydride can be made by direct reaction of Lithium hydride with tri-sec-butyl borane only in poor yield^{147,148}.

$\text{LiH} + (\text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3))_3\text{B} \rightarrow \text{Li}(\text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3))_3\text{BH}$ (~ 10% yield); the preferred synthesis is the reaction of the borane with Lithiumaluminium hydride^{149,150}.

Unlike the lithium and sodium compounds the potassium tri-sec-butylborohydride is easily made by the reaction of potassium hydride with tris(1-methylpropyl)borane¹⁵¹.

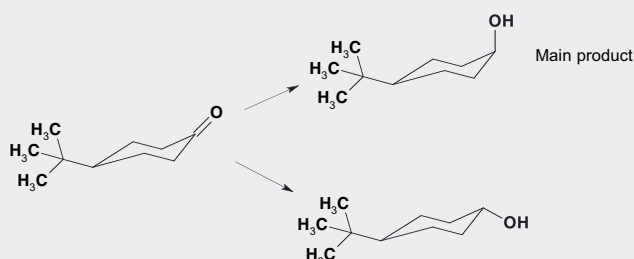


The tri sec-butyl borohydrides are strong reducing agents and have been used in many regio- and stereoselective reductions¹⁵². Alkylhalides are reduced to the alkanes¹⁵³ but the main application is the chemo-, regio- and stereoselective reduction of carbonyl compounds:

Ketones are reduced chemoselectively by lithium tri sec-butylborohydride in the presence of other reducible functional groups like carboxylic acids¹⁵⁴ and esters¹⁵⁵.

It reduces aldehydes, ketones and acid chlorides rapidly to the aldehydes.

The stereoselective reduction of tert-butylcyclohexanone^{147, 150} leads in contrast to other hydride-reducing agents⁴⁷ to the thermodynamically less stable axial alcohol.



Deuterated lithium tri sec-butylborodeuteride has been used for the stereoselective reduction of cyclohexanones¹⁵⁶.

¹⁴⁷ H.C. Brown, S. Krishnamurthy, J. Am. Chem. Soc. 94 (1972) 7159.

¹⁴⁸ H.C. Brown, S. Krishnamurthy, J.L. Hubbard, J. Am. Chem. Soc. 100 (1978) 3343.

¹⁴⁹ H.C. Brown, J.L. Hubbard, B. Singaram, Tetrahedron 37 (1981) 2359.

¹⁵⁰ H.C. Brown, J.L. Hubbard, B. Singaram, J. Org. Chem. 44 (1979) 5004.

¹⁵¹ H.C. Brown, S. Krishnamurthy, J. Org. Chem. 51 (1986) 238.

¹⁵² S. Wittmann, B. Schönecker, J. Prakt. Chem. 338 (1996) 759.

¹⁵³ S. Kim, K.Y. Yi, Bull. Chem. Soc. Jp. 58 (1985) 789.

¹⁵⁴ M.J. Arco, M.H. Trammell, J.D. White, J. Org. Chem. 41 (1976) 2075.

¹⁵⁵ A.E. Greene, M.-J. Luche, A.A. Serra, J. Org. Chem. 50 (1985) 3957.

¹⁵⁶ P. Gärtner, C. Novak, M. Knollmüller, G. Gmeiner, Arkivoc 2001 (II) 9.



Diastereoselective reduction of chiral β,γ -unsaturated- α -oxo-esters¹⁵⁷.

Products from Acros Organics	
Lithium tri-sec-butylborohydride, 1M solution in THF	17645
Sodium tri-sec-butylborohydride, 1 M solution in tetrahydrofuran	20002
Potassium tri-sec-butylborohydride, 1 M solution in tetrahydrofuran	20547

3.7.3. Lithium trisamylborohydride

Lithium trisamylborohydride is an extremely sterically hindered borohydride which is still a powerful reducing agent¹⁵⁸.

Products from Acros Organics	
Lithium trisamylborohydride, 1M solution in THF	20968

3.8. Alkylsubstituted aluminiumhydrides

Diisobutylaluminium hydride (DIBAL-H) is a clear colorless liquid (boiling point 270 °C, 116-118°C /1 mm, d: 0,798 g/ml) which spontaneously ignites on contact with air and which violently reacts with water and other protic solvents. Also DIBAL-H solutions with a concentration above 25wt% should be considered as pyrophoric¹⁵⁹.

It is available as solution in aliphatic and aromatic hydrocarbons like toluene, hexane, heptane, cyclohexane and also in dichloromethane and THF, but ethers like THF are problematic solvents since they can react with the reagent at elevated temperatures¹⁶⁰.

DIBAL-H is soluble in all aliphatic and aromatic hydrocarbons and miscible in all ratios. The dissolution of DIBAL-H in etheral solvents is an exothermic reaction and due to the complex formation in ethers, it is a weaker reducing agent in these solvents.

DIBAL-H^{161,162} reduces aldehydes, ketones acids esters and acid chlorides to the corresponding alcohols, amides are reduced to amines.

¹⁵⁷ H. Sugimura, K. Yoshida, J. Org. Chem. 58 (1993) 4484.

¹⁵⁸ S. Krishnamurthy, H.C. Brown, J. Am. Chem. Soc. 98 (1976) 3383.

¹⁵⁹ Akzo Nobel: Technical Bulletin: „Diisobutylaluminium hydride (DIBAL-H) and Other Isobutyl Aluminium Alkyls (DIBAL-BOT, TIBAL) as Specialty organic Synthesis reagents“.

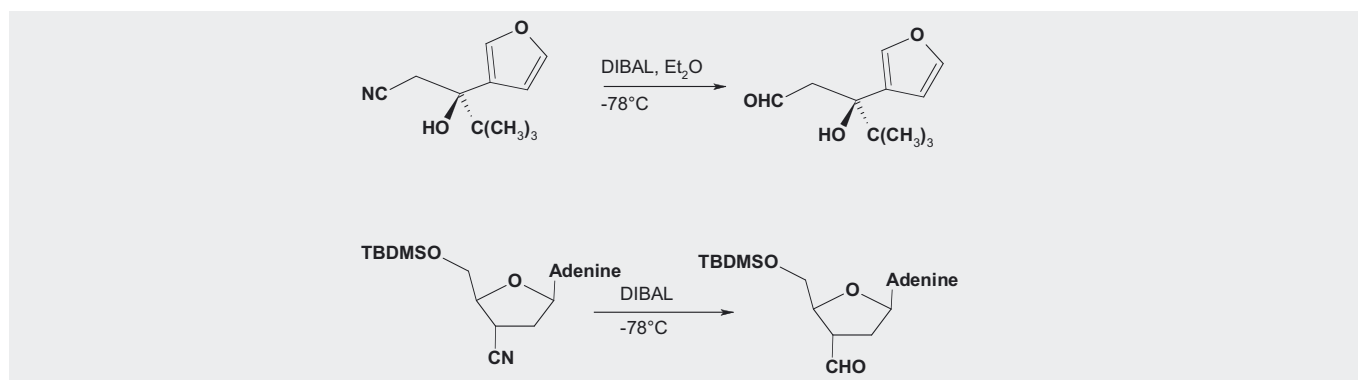
¹⁶⁰ E. Winterfeld, Synthesis (1975) 617.

¹⁶¹ N.M. Yoon, Y.S. Gyoung, J. Org. Chem. 50 (1985) 2443.

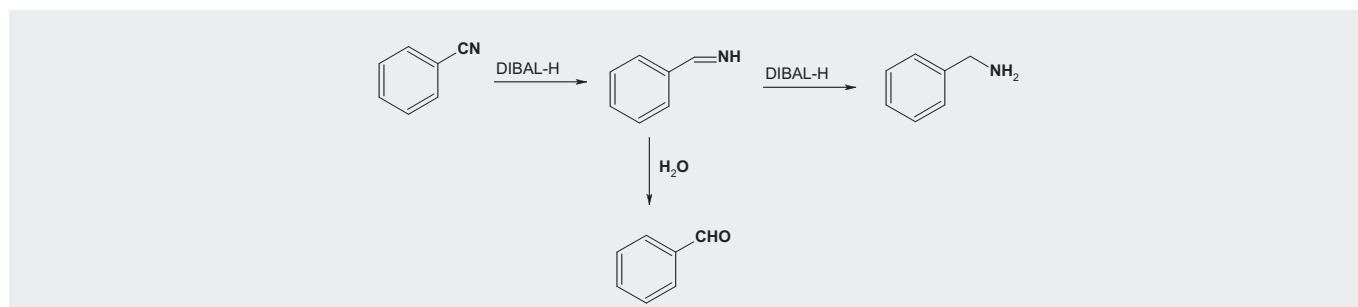
¹⁶² I. Fernandez-Bachiller, Synlett, 2002 179.



Nitriles react with DIBAL to furnish imines as intermediates which are hydrolyzed to aldehydes^{163, 164, 165, 166}.

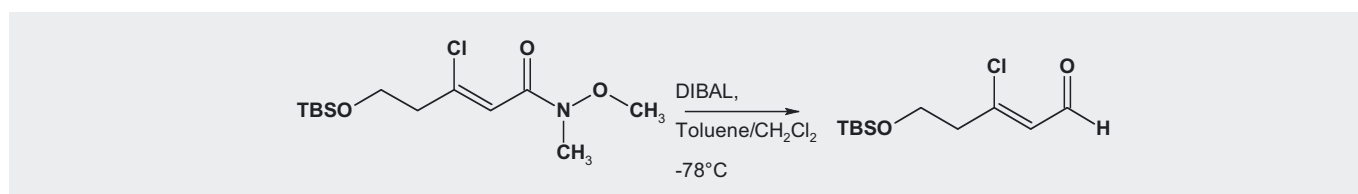


With two equivalents of DIBAL-H at higher temperatures Benzonitril was reduced directly to the Benzylamine.



The selective reduction of esters and amides to aldehydes^{167, 168} at low temperatures is probably the most commonly used application of diisobutylaluminium hydride.

N-Methoxy-N-methyl carboxamides ("Weinreb amides") are readily converted to aldehydes¹⁶⁹.



Aryl- and alkylhalides do not react with DIBAL¹⁶¹, but primary alkyl-tosylates react readily to the alkanes while other alkyltosylates give elimination products.

An "ate" complex from DIBAL with n-butyllithium has been used for the reduction of a range of primary and secondary alkyl and benzylic halides¹⁷⁰.

¹⁶³ J.A. Marshall, N.H. Andersen, J.W. Schlicher, J. Org. Chem. 35 (1970) 858.

¹⁶⁴ A.E.G. Miller, J.W. Biss, L.H. Schwartzman, J. Org. Chem. 24 (1959) 627-630.

¹⁶⁵ M.T. Crimmins, D.K. Jung, J.L. Gray, J. Am. Chem. Soc. 115 (1993) 3146.

¹⁶⁶ D. Yu, M. d'Alarcao, J. Org. Chem. 54 (1989) 3240.

¹⁶⁷ C. Szantay, L. Toke, P. Kolonits, J. Org. Chem. 31 (1966) 1447.

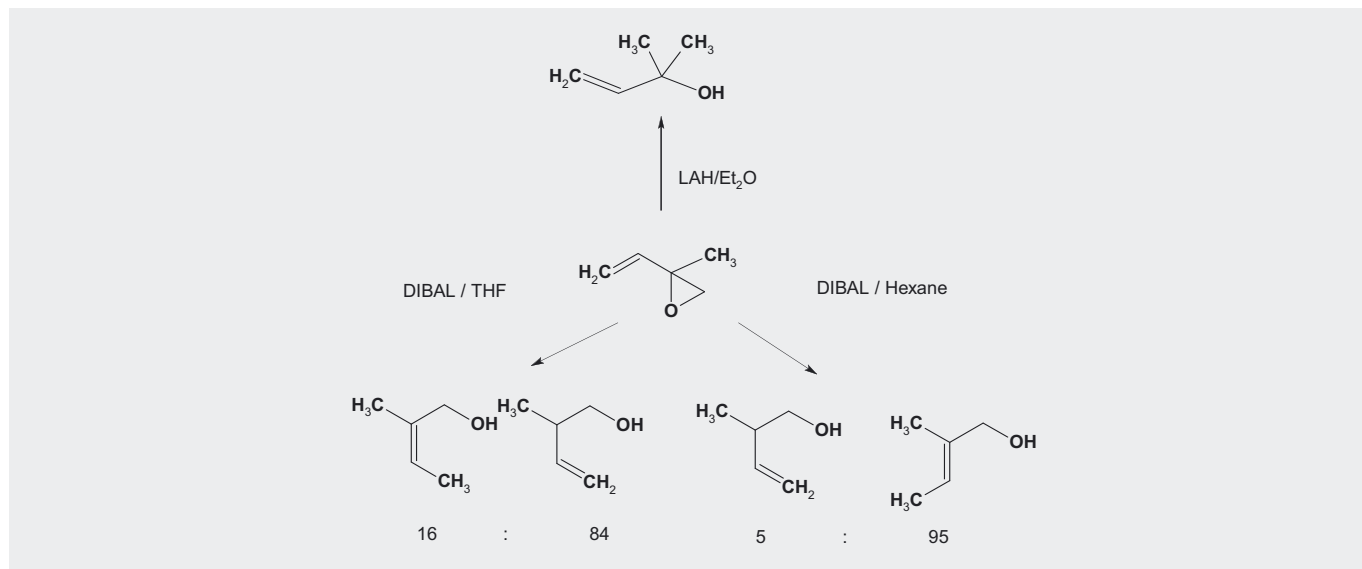
¹⁶⁸ J. March, Advanced Organic Chemistry, Fourth Edition, John Wiley Sons 1992, p 397-398.

¹⁶⁹ D. Trauner, J.B. Schwarz, S.J. Danishefsky, Angew. Chem. 111 (1999) 3756.

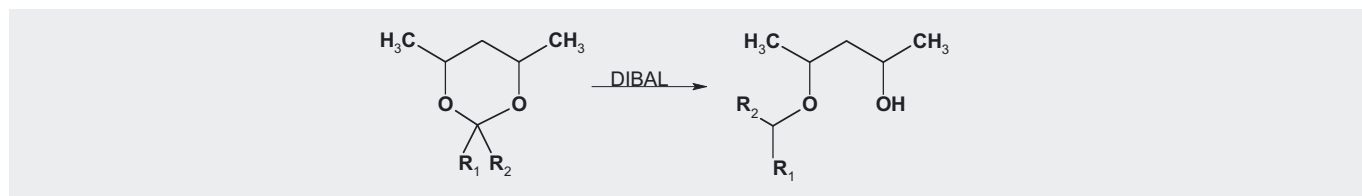
¹⁷⁰ S. Kim, K.H. Ahn, J. Org. Chem. 49 (1984) 1717.



Epoxides are opened by DIBAL, but the regioselectivity of the reaction is different from the ring-opening reaction by lithium aluminium hydride¹⁷¹. The product distribution indicates that a DIBAL reacts with the epoxides first as a Lewis acid, leading to a carbenium-ion-like intermediate, which in a second step is reduced by the hydride. This stands in contrast to the reduction with LAH.

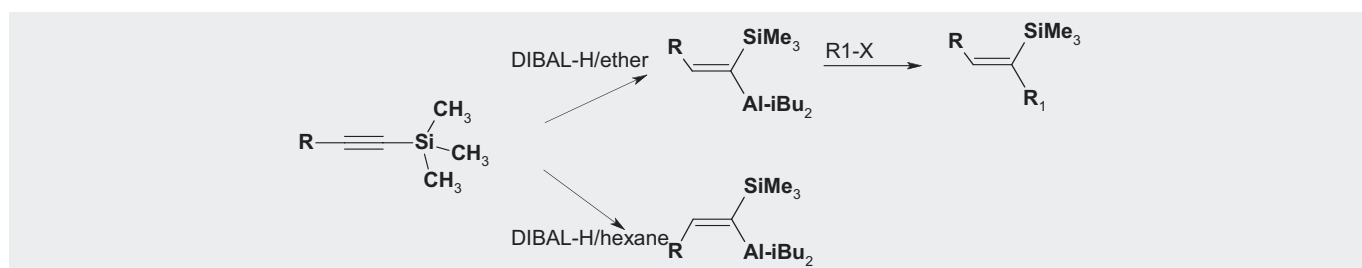


The Lewis acidity of DIBAL is also responsible for the reductive cleavage of acetals¹⁷² and the reactivity towards ethers at higher temperatures.



DIBAL is a very valuable reagent for the selective 1,2-reduction of α,β -unsaturated ketones to allylic alcohols¹⁷³.

Another important reaction of DIBAL-H is the selective reduction of acetylenes to cis-olefins via "hydroalumination"^{174,175}.



¹⁷¹ R.S. Lenox, J.A. Katzenellenbogen, J. Am. Chem. Soc. 95 (1973) 957.

¹⁷² A. Mori, J. Fujiwara, K. Maruoka, H. Yamamoto, Tetrahedron Lett., 24, (1983) 4581.

¹⁷³ K.E. Wilson, R.T. Seidner, S. Masamune, J. Chem. Soc. Chem. Comm. (1970) 213.

¹⁷⁴ G. Zweifel, R.L. Milier, J. Am. Chem. Soc., 92 (1970) 6678.

¹⁷⁵ H. Yamamoto, Organoaluminium Compounds in Organometallics in Synthesis, M. Schlosser (ed) John Wiley and sons 1994.



Products from Acros Organics

Diisobutylaluminium hydride, 1M solution in hexane	18379
Diisobutylaluminium hydride, 20 wt% solution in toluene, 1,2M	20108
Diisobutylaluminium hydride, 1.1M solution in cyclohexane	20103
Diisobutylaluminium hydride, 1.0M solution in heptane	20105



Name	Product code	Page
Benzyltriethylammonium borohydride 96%	30247	19
Benzyltriphenylphosphonium borohydride 95%	37637	19
1,1'-Bi-2-naphthol 99%	14735	10
(R)-(+)-1,1'-Bi-2-naphthol 99%	22430	10
(S)-(-)-1,1'-Bi-2-naphthol 99%	22431	10
Bis(cyclopentadienyl)dimethyltitanium, 5 wt% in toluene	30176	6
Bis(cyclopentadienyl)dimethylzirconium	34789	6
Bis(cyclopentadienyl)titanium dichloride 97%	21576	6
Bis(cyclopentadienyl)titanium dichloride 99%	37246	6
Bis(cyclopentadienyl)titanium(III) chloride 96%	37574	6
Bis(cyclopentadienyl)vanadium 95%	35340	6
Bis(cyclopentadienyl)vanadium dichloride 95%	35341	6
Borane-dimethylamine complex 98+%	17731	3
Borane-methyl sulfide complex 94%	17706	3
Borane-methyl sulfide complex, 1M solution in methylene chloride	18561	3
Borane-methyl sulfide complex, 2M solution in tetrahydrofuran	18507	4
Borane-morpholine complex 97%	17729	4
Borane-N,N-diethylaniline complex 97%	17677	3
Borane-pyridine complex 95%	17701	4
Borane-tert-butylamine complex, pellets	18922	3
Borane-tert-butylamine complex, powder 95%	17730	3
Borane-tetrahydrofuran complex, 1M solution in THF, stabilized	17508	4
Borane-triethylamine complex 99%	40273	4
Borane-trimethylamine complex 98%	40274	4
Borane-triphenylphosphine complex 97%	22300	4
Diethylaluminium chloride, 0.9M solution in toluene	38115	6
Diethylaluminium chloride, 1.1M solution in toluene	18544	6
Diethylaluminium chloride, 1M solution in hexanes	19952	6
Diisobutylaluminium hydride, 1.0M solution in heptane	20105	33
Diisobutylaluminium hydride, 1.1M solution in cyclohexane	20103	33
Diisobutylaluminium hydride, 1M solution in hexane	18379	33
Diisobutylaluminium hydride, 20 wt% solution in toluene, 1,2M	20108	33
Lithium aluminium deuteride 98 atom% D, for NMR	18567	11
Lithium aluminium hydride 95%, in resealable tin cans	33210	11
Lithium aluminium hydride 95%, pellets	30453	11
Lithium aluminium hydride 95%, powder	19032	11
Lithium aluminium hydride, 1,0M solution in THF	19949	11
Lithium aluminium hydride, 15% solution in toluene/THF	38557	11



Name	Product code	Page
Lithium aluminium hydride, 2.4M solution in THF	37732	11
Lithium aluminium hydride, 4.0M solution in diethyl ether	19951	11
Lithium borohydride 95%,	20681	18
Lithium borohydride, 2M solution in tetrahydrofuran	21293	18
Lithium triethylborohydride, 1M solution in THF	17699	28
Lithium tri-sec-butylborohydride, 1M solution in THF	17645	30
Lithium trisiamylborohydride, 1M solution in THF	20968	30
Lithium tri-tert-butoxyaluminumhydride 93-98%	12516	25
Lithium tri-tert-butoxyaluminumhydride, 1.1M solution in THF	37758	25
4-Methylbenzenesulfonhydrazide 97%	15786	21
Potassium borohydride 98%,	19665	18
Potassium triethylborohydride, 1 M solution in tetrahydrofuran	20004	28
Potassium tri-sec-butylborohydride, 1 M solution in tetrahydrofuran	20547	30
Silicagel, functionalized,(trimethylammonium)propyl cyanoborohydride, ca. 1	37154	21
Sodium aluminium hydride 93%	38011	11
Sodium bis(2-methoxyethoxy)aluminiumhydride, 70 wt% sol. in toluene (ca.	18790	26
Sodium borodeuteride 98 atom% D, for NMR	19495	16
Sodium borohydride 98%, (12-13 mm), pellets, 7/16"	20148	16
Sodium borohydride 98%, granules, ca 3 mm	41947	16
Sodium borohydride 98+%, powder	18930	16
Sodium borohydride 99%, powder	20005	16
Sodium borohydride, 0.5 M solution in diglyme	19113	16
Sodium borohydride, 12% solution in 40% aq. sodium hydroxide solution	38993	16
Sodium cyanoborohydride 95%	16855	21
Sodium tetraethylborate 97%	36388	4
Sodium triacetoxyborohydride 97%	29182	23
Sodium triethylborohydride, 1 M solution in tetrahydrofuran	20003	28
Sodium tri-sec-butylborohydride, 1 M solution in tetrahydrofuran	20002	30
Tetrabutylammonium borohydride 98%	21290	19
Tetraphenylboron sodium, p.a.	13852	4
Tetraphenylboron sodium, reagent ACS	42445	4
Titanium(III) chloride, 30 wt% solution in 2N hydrochloric acid	23550	6
Titanium(III)chloride 98%, Al reduced	33152	6
Titanium(IV) chloride 99.90%	19723	6
Titanium(IV) chloride, 1M solution in dichloromethane	37774	6
Titanium(IV) chloride, 1M solution in toluene	37816	6
Vanadium(IV) chloride 99+%	29969	6



ALUMINIUM

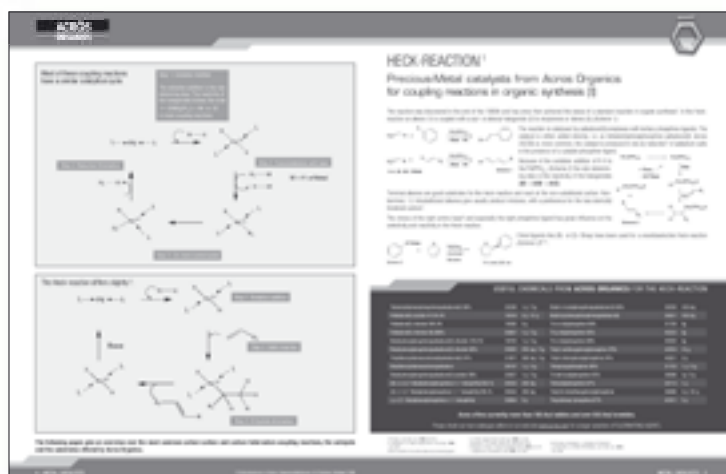
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