Kemira Sodium Borohydride $NaBH_4$ |

An effective reducing agent

Sodium Borohydride $NaBH_4$

An effective and selective reducing agent

$NaBH_4$ is a very effective and selective reducing agent. It is widely used in its dry form (white crystalline powder or granules) by the pharmaceutical and fine chemical industry in applications where an excellent hydrogenation and reduction is needed. The reductions can be carried out with a wide range of carbonyl substrates and the products are often building blocks especially for the synthesis of pharmaceutically active compounds.

$NaBH_4$ is also used to purify organic chemicals by removing metal ions, carbonyl and peroxide impurities that cause undesirable odor, taste, color and instability to products.

Sodium borohydride is easy to handle when the appropriate safety precautions are followed. It is not necessary to exclude moisture nor atmospheric oxygen when using $NaBH_4$. The water present in the reaction mixture usually does not have unfavourable effects on the desired reduction, provided that there is sufficient borohydride present. This is the main reason why a slight excess of sodium borohydride is used customarily in reduction reactions.

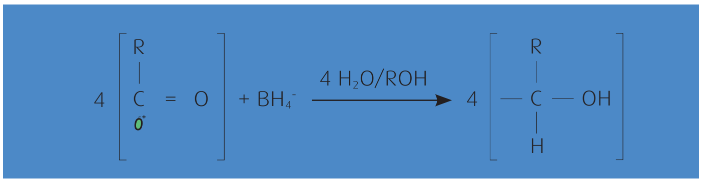
$NaBH_4$ is above all used for reducing aldehydes and ketones. Aldehydes can be reduced selectively in the presence of ketones. In alcoholic media or THF sodium borohydride reduces for example halides, anhydrides, quartenary pyridinium salts, double bonds conjugated to two electron-withdrawing groups and C-Hg bonds. It leaves under ambient conditions epoxides, esters and lactones, carboxylic acids, amides and most nitro compounds unreacted.

The reactivity of $NaBH_4$ can be enhanced by using additives. In the presence of organic acids $NaBH_4$ forms acyloxyborohydrides, either monoacyloxy ($Na(RCOO)BH_3$) or triacyloxyborohydrides ($Na(RCOO)_3BH$) depending on the quantity of organic acid (RCOOH) present.

Reduction of organic compounds

In organic reactions the reduction occurs on the carbon atom having the highest positive partial charge. The rate of reduction is increased by any substituent that increases the partial positive charge of the carbonyl carbon. The reductions of carbonyl groups by borohydride occur mostly by nucleophilic attack of hydride on the carbonyl carbon.

The basic reduction mechanism of sodium borohydride.



$$4\left[\overset{R}{\underset{\delta^+}{C}} = O\right] + BH_4^- \xrightarrow{4\ H_2O/ROH} 4\left[-\overset{R}{\underset{H}{C}}-OH\right]$$

The mechanism shows that 1 mol of $NaBH_4$ can reduce as many as four molecules of a carbonyl compound. Four molecules of water or alcohol is needed to hydrolyze the formed tetraalkoxyborate. Because $NaBH_4$ is highly reactive to the positive charge of the carbonyl carbon, the aldehydes can be reduced selectively in the presence of other functional groups, for example ketones, esters, imides and nitriles.

Other applications

Organoboranes

Organoboranes are prepared by borane (BH_3) which undergoes rapid and quantitative hydroboration with most alkenes to form organoboranes (R_3B). Organoboranes are important reactive intermediate products widely used in organic synthesis, e.g the reduction of α-amino acids to α-amino alcohols as these are important intermediates in the synthesis of many pharmaceutically active compounds.

The borane needed for the reaction is often prepared in situ by the reaction of $NaBH_4$ and a Lewis acid such as BF_3, $AlCl_3$, I_2 or Me_3SiCl.

$$2\ NaBH_4 + I_2 \xrightarrow{diglyme} 2\ NaI + B_2H_6 + H_2$$

The reaction produces diborane (B_2H_6), which is a gaseous dimeric form of borane. Borane is generally employed as a solvate with THF or Me_2S.

Organometallic reactions

The applications of sodium borohydride on organometallic reactions can in general be divided into four major types:

1) initial formation of organometallic compounds and complexes
2) reductions to lower-valent metal compounds
3) demetallation or cleaveage of organometallic compounds to the metal and organic species, e.g reduction of organomercurials to saturated functionalized compounds
4) conversion of organometallic halides to the corresponding hydride or hydride halide.

Metal cations reductions

Sodium borohydride solution is used to purify waste waters and product streams by reducing soluble metal ions to insoluble elemental metals, which may then be separated from the solution by filtration or decantation. Toxic and valuable heavy metals such as lead, mercury, gold, silver, and platinum are recovered by $NaBH_4$ reduction. When sodium borohydride is dissolved in a suitable solvent, eight electrons per molecule become available for reduction.

$$NaBH_4 + 2H_2O \longrightarrow NaBH_2 + 8\,H^+ + 8\,e^-$$
$$8\ Me^+ + 8\ e^- \longrightarrow 8\ Me^0$$

Theoretically the following quantities of metals can be reduced by 1 kg of sodium borohydride, but in practice certain additional dosage of $NaBH_4$ is needed to gain good yields. When the conditions are right, the efficiency is good and the reduction is complete.

The theoretical amounts of sodium borohydride needed to reduce metal cations.

METAL		kg metal /kg $NaBH_4$	kg $NaBH_4$ /kg metal
Cadmium	Cd^{2+}	11,9	0,085
Cobalt	Co^{2+}	6,2	0,161
Copper	Cu^{2+}	6,7	0,147
Gold	Au^{3+}	13,7	0,073
Iridium	Ir^{4+}	10,1	0,099
Lead	Pb^{2+}	21,9	0,046
Mercury	Hg^{2+}	21,2	0,048
Nickel	Ni^{2+}	6,2	0,162
Platinium	Pt^{4+}	10,3	0,097
Rhodium	Rh^{3+}	7,2	0,138
Silver	Ag^{+}	22,8	0,044

Sodium Borohydride $NaBH_4$ – Powder, granules

Chemical and physical properties

Chemical name	Sodium borohydride
Chemical formula	$NaBH_4$
Molecular weight	37.84 g/mol
Purity	min 98 %

Typical content

$NaBH_4$	98.4 – 99.5 %
	$NaBO_2$ < 1.5 %
	NaOH < 0.1 %
	H_2O < 0.1 %

Theoretical hydrogen content 10.6 w- %

Typical properties

Appearance	white crystalline solid
Bulk density approx.	400 kg/m³ for powder 510 kg/m³ for granules 550 kg/m³ for tablets
Melting point	~ 500 °C at 2 – 6 bar H_2
Decomposes	above 400 °C in vacuum

Crystal form (anhydrous) face centered cubic (NaCl structure) a0 = 6.14 Å

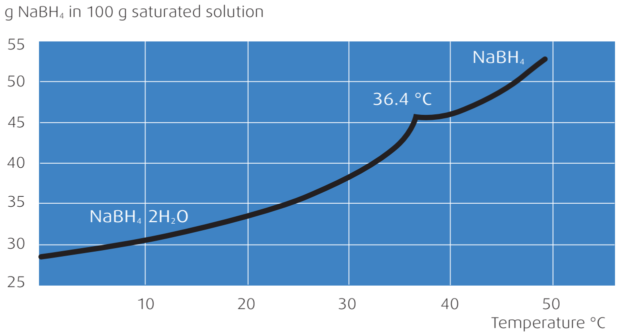
Analytical methods

The sodium borohydride assay can be determined either by iodometric titration or gas evolution method. We are glad to provide details about these analysis methods upon request.

Solubility in water

Sodium borohydride crystallizes in dihydrate form in water on temperatures below 36.4 °C and in anhydrous form on temperatures over it. The following diagram shows the equilibrium temperature of the two crystal forms of $NaBH_4$.

Solubility of sodium borohydride in water at different temperatures.

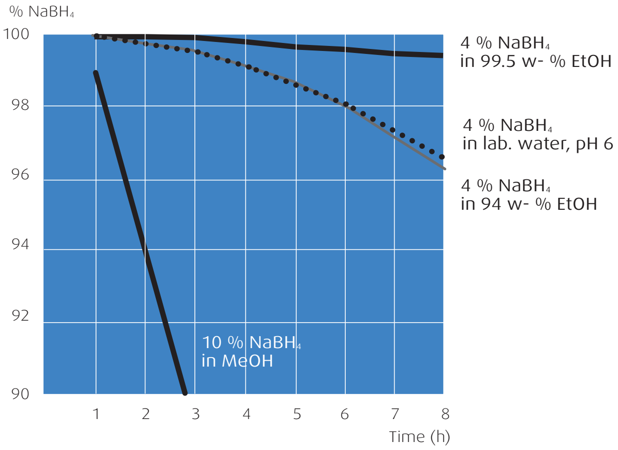


Solubility in organic solvents

Sodium borohydride is soluble in most polar solvents that contain a hydroxyl or an amine group. **Appendix 1** contains more information about the solubility of $NaBH_4$.

The stability of sodium borohydride in organic solvents is dependent on the degree of hydrolysis that can occur. Sodium borohydride instability in lower alcohols (methanol, ethanol) can be overcome by the addition of a base. The presence of water accelerates the hydrolysis reaction.

Stability of sodium borohydride in different solvents at room temperatures.



Delivery and transport regulations

Standard packaging

10 kg plastic bags in steel drums of 10 kg, 40 kg or 50 kg

Transport regulations

UN No	1426
IMDG class	4.3/I
ADR/RID class	4.3/I
ICAO/IATA	4.3/I CAO 412, PAX F

Toxicity

LD50	18 mg/kg ipr/rat
	4 – 8 g/kg dermal/rabbit

CAS No	16940-66-2
EINECS No	241-004-4

Handling and storage

$NaBH_4$ is safe to handle and use when certain normal industrial safety regulations are followed. It is chemically stable under normal conditions and in unopened drums. Sodium borohydride must be stored in closed vessels in a dry, cool and well-ventilated area, where the relative humidity in the air is preferably below 20 %.

It must be kept separate from

- acids
- oxidizing substances
- heavy metal salts
- open fire and heat sources.

$NaBH_4$ may liberate hydrogen gas even violently or explosively when reacting with oxidizers, acids, heavy metals or heavy metal salts. Contact with moisture, water or steam causes gradual decomposition of the product and a slow release of hydrogen. Hydrogen is highly flammable and can form an explosive mixture with air. In reactions with acids or in acidic conditions borohydride products can generate heat and liberate hydrogen gas.

The powder ignites from free flame in the air and will continue to burn as hydrogen is evolved from the decomposition. If it has caught fire, do not use water or carbon dioxide for extinguishing. Dry sand, powdered limestone or dry extinguishers with sodium chloride or anhydrous sodium carbonate are most suitable.

Protective clothing, plastic or rubber gloves and boots, eye or face protector and dust mask shall always be used when handling the product. Also sufficient ventilation is recommended.

First aid

Dry sodium borohydride products are corrosive to the eyes, skin and respiratory tract. Moisture increases the toxicity and can result in severe irritation and skin burns.

Inhalation

Move to fresh air and rinse mouth with water. Consult a physician.

Eye contact

Rinse thoroughly with running water for at least 15 minutes and consult a physician.

Skin contact

Wash off immediately with plenty of water for at least 15 minutes. Remove contaminated clothing and shoes. Cleanse skin with soap and water including hair and under fingernails. If irritation develops, consult a physician.

Ingestion

Rinse mouth with water and immediately give several glasses of water to drink. Seek medical advise immediately. Prevent vomiting if possible.

Disposal

Dispose sodium borohydride according to the local legislation. Small amounts of sodium borohydride can be disposed by dilution with large excess of water followed by slowly adding dilute acetic acid or acetone solution to the neutral pH. Do not flush sodium borohydride into the sewer. The procedure must be carried out carefully in a well-ventilated place because of the liberating hydrogen gas by exothermic hydrolysis reaction.

$$\mathbf{NaBH_4 + 2H_2O \longrightarrow NaBO_2 + 4\ H_2}$$

$$\mathbf{\Delta H° = -218\ kJ\ mol^{-1}}$$

Before using sodium borohydride please check carefully the information on handling and precautions from the Safety Data Sheet of our product. The instructions of the local authorities are to be observed.

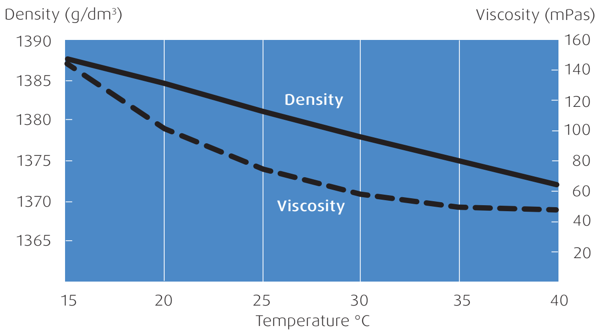
Sodium Borohydride $NaBH_4$ Solution

Chemical and physical properties

Typical content	$NaBH_4$	12.0 %
	NaOH	40.0 %
	balance	H_2O
Alkalinity	pH approx. 14	
Appearance	colorless liquid	

Crystallizes below 10 °C (50 °F), can be liquefied again by warming slowly.

Sodium borohydride density and viscosity varies at different temperatures.

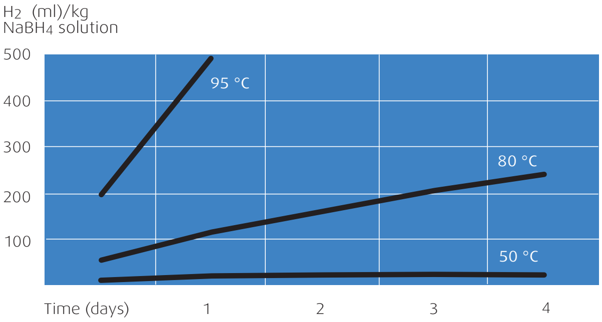


We also prepare sodium borohydride solutions for customers´ special needs, for example Hydrifin C concentrate containing 20 % $NaBH_4$ and 20 % NaOH, balance water.

Stability

The stability of sodium borohydride in solution that contains water is dependent upon the temperature and pH of the solution. The hydrolysis reaction occurs evolving hydrogen gas decreasing the stability of sodium borohydride, when temperature is increased or pH is lowered.

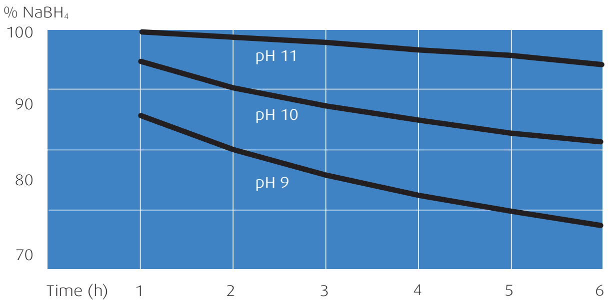
Stability of sodium borohydride 12 % solution at different temperatures.



The pH rose from the starting pH values 9 and 10 to near pH 11 during the decomposition reaction. The increase of the pH was caused by the formation of the strongly basic metaborate ion and it effected by decreasing the initial rate of hydrogen evolution.

$$\mathbf{BH_4^- + 2H_2O \longrightarrow BO_2^- + 4\,H_2}$$

The stability of 1 mol/l sodium borohydride water solution at different pH at room temperatures.



Delivery and transport regulations

Packaging

Bulk tank containers
IBC-containers 1400 kg
PE-plastic drums 300 kg

Packaging materials

Suitable materials for storage tanks and vessels are stainless steel as well as alkaline resistant plastics. Aluminium and zink are not acceptable.

Transport regulations

UN No	3320
IMDG class	8/II
ADR/RID class	8/II

Toxicity

The solution irritates and burns the skin and the mucous membranes. Very hazardous in contact with eyes.

$NaBH_4$	
LD_{50}	18 mg/kg ipr/rat
CAS No	16940-66-2
EINECS No	241-004-4

NaOH	
LD_{50}	140–340 mg/oral/rat
CAS No	1310-73-2
EINECS No	215-185-5

Handling and storage

Sodium borohydride solution is stable under normal conditions, the decomposition is less than 0.1 % per year. During long storage periods hydrogen may evolve solution into the space above. Keep the containers in cool, dry and well ventilated place away from water, acids (reacts vigorously generating heat and hydrogen gas), oxidizing substances (reacts violently or explosively) and chemically active metals (reacts releasing hydrogen).

A ventilation line out is recommended. All closed containers should have at least 10 % free volume and they should be checked periodically. The recommended storage temperature is 20 – 25 °C (68 – 77 °F). Recommended storage materials are stainless steel and alkaline resistant plastics. Check also the suitability of sealing materials with caustic.

Protective clothing, plastic or rubber gloves and boots and eye or face protector should always be used when handling the product. Please note that sodium borohydride solution is strongly alkaline and corrosive.

First aid

The sodium borohydride solution irritates and burns the skin and the mucous membranes. It is especially hazardous in contact with eyes.

Inhalation
Move to fresh air and rinse mouth with water. Consult a physician.

Eye contact
Immediately rinse thoroughly with running water for at least 15 minutes and consult always a physician.

Skin contact
Wash off immediately with plenty of water for at least 15 minutes. Remove contaminated clothing and shoes. Cleanse skin with soap and water including hair and under fingernails. If irritation develops consult a physician.

Ingestion
Rinse mouth with water and immediately give several glasses of water to drink. Seek medical advise immediately. Prevent vomiting if possible.

Disposal

Dispose sodium borohydride solution according to the local legislation. Small amounts of sodium borohydride can be disposed by dilution with large excess of water and neutralization of the sodium hydroxide with dilute inorganic acids. Because flammable hydrogen gas is evolving during neutralization it should be done in a well ventilated area (fume hood) without open fire or any ignition sources nearby. The hydrolysis reaction is exothermic.

Before using sodium borohydride please check carefully the information on handling and precautions from the Safety Data Sheet of our product. The instructions of the local authorities are to be observed.

Derivatives of Sodium Borohydride

Sodium triacetoxyborohydride

$NaBH(CH_3COO)_3$

CAS Registry No: 56553-60-7

Product description

Sodium triacetoxyborohydride is a mild and selective reducing agent. It is able to replace toxic sodium cyanoborohydride under most conditions. It is selective in reducing aldehydes to alcohols in the presence of ketones. STAB is also stable in anhydrous acids, which enables reductive amination of aldehydes and ketones. The advantage of STAB compared to sodium cyanoborohydride is evident. STAB, being non-toxic, is easier to handle and forms no toxic by-products, making the treatment of wastes after the reaction simple and less costly.

Product properties

Sodium triacetoxyborohydride content	min 95 %
Method of analysis	Gas-volumetric method
Molecular weight	211,94 g/mol
Relative density	1,374 kg/dm³
Appearance	white powder

Delivery and transport regulations

Standard packing 3 x 10 kg PE bag in steel drum. Delivery by road, sea and air.

Shipping name	Sodium triacetoxy borohydride
UN Number	2813
Hazard Class	4.3
Packing Group	I

Storage and handling

Keep tightly closed in a dry, cool and well-ventilated area. STAB decomposes in contact with water or moisture releasing flammable hydrogen gas. It also decomposes when heated above 80°C. Keep away from open flames, hot surfaces and sources of ignition. Keep under nitrogen. Keep away from acids, oxidizing agents and alcohols.

Before using borohydride products please check carefully the information on handling and precautions from the Safety Data Sheet of our products. The instructions of the local authorities are to be observed.

Appendix1. Solubility of sodium borohydride (g/100 g of solvent).

Solvent	Boiling point of solvent °C	Temperature °C	Solubility g NaBH$_4$/100 g solvent
Water	100.0	0	25.0 (decomp.)[a]
		25	55.0 (decomp.)[a]
		60	88.4 (decomp.)[a]
Methanol	64.7	20	16.4 (decomp.)[a]
Ethanol	78.5	20	4.0 (decomp.)[a]
Isopropanol	82.5	20	0.25
		60	0.88
Tert. Butanol	82.5	25	0.11
		60	0.18
Tetrahydrofurfuryl Alcohol	177.0	20	14.0 (decomp.)[a]
Ammonia, liquid	-33.3	25	104.0
Methyl Amine	-6.5	-20	27.6
Dimethyl Amine	6.8	2	4.0
Ethyl Amine	16.6	17	20.9
Diethyl Amine	55.2	20	1.0
Triethyl Amine	89.3	20	1.0
N-propyl Amine	48.7	28	9.7
Isopropyl Amine	34.0	28	6.0
N-butyl Amine	77.8	28	4.9
Cyclohexyl Amine	134.5	28	1.8
Monoethanol Amine	170.0	25	7.7
Ethylene Diamine	118.0	75	22.0
Morpholine	128.3	25	1.4
Pyridine	115.3	25	3.1
		75	3.4
Acetonitrile	82.0	28	0.9
Dimethyl Formamide (DMF)	153.0	20	18.0[b]
Dimethyl Sulfoxide (DMSO)	100.0	25	5.8 (decomp.)[a]
Tetrahydrofurane (THF)	65.0	20	0.1
Ethylene Glycol Dimethyl Ether (monoglyme)	85.0	0	2.6
		20	0.8
Diethylene Glycol Dimethyl Ether (diglyme)	162.0	0	1.7
		25	5.5
		40	11.0
		45	8.0
		75	0.0
Triethylene Glycol Dimethyl Ether (triglyme)	216.0	0	8.4
		25	8.7
		50	8.5
		100	6.7
Tetraethylene glycol dimethyl ether (tetraglyme)	275.8	0	8.7
		25	9.1
		50	8.4
		75	8.5
		100	4.2
Ethylene glycol monomethyl ether	125.0	100	16.7

a) Decomposition can occur liberating hydrogen; ensure ventilation.

b) Caution: can react violently at higher temperatures.

Hydrifin products

Our wide range of Hydrifin products for the pharma and fine chemicals industries include:

Hydrifin P (powder)
sodium borohydride min. 98,0 %
particle size 0,01-0,1 mm

Hydrifin GS (semigranular)
sodium borohydride min. 98,0 %
particle size 0,1-1,0 mm

Hydrifin G (granular)
sodium borohydride min. 98,0 %
particle size 1,0-3,0 mm

Hydrifin T (tablets)
sodium borohydride min. 98,0 %
tablet diameter 20 mm

Hydrifin L (solution)

sodium borohydride	12,0 %
sodium hydroxide	40,0 %
water	48,0 %

Hydrifin C (concentrate)

sodium borohydride	20,0 %
sodium hydroxide	20,0 %
water	60,0 %

Hydrifin STAB
sodium triacetoxyborohydride min. 95,0 %

TMB
Trimethyl borate min. 70%, 98,5% and 99,8% grades

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